Washington State Health Care Authority
Prescription Drug Program
P.O. Box 91132 • Seattle, Washington 98111-9232
206-521-2027 • FAX 206-521-2001 • TTY 360-923-2701 • www.rx.wa.gov

UNOFFICIAL TRANSCRIPT*
WASHINGTON STATE
PHARMACY AND THERAPEUTICS COMMITTEE MEETING

October 20, 2010
Sea Tac Marriott Hotel
9:00am – 4:00pm

Vyn Reese: This is Dr. Reese. I'd like to have everyone take their seats, please.

The State Pharmacy and Therapeutics Committee will now come to order. Welcome. I'd like to start the meeting with introductions and I'll begin on my left.

Amy Irwin: Amy Irwin, Medicaid Purchasing Administration.

Chuck Agte: Chuck Agte, Pharmacy Program Manager for Medicaid Purchasing Administration.

Cathy Williams: Cathy Williams, Pharmacist Consultant, Board of Pharmacy.

Jaymie Mai: Jaymie Mai, Labor and Industries.

Doug Tuman: Doug Tuman, L&I.

Jeff Graham: Jeff Graham, Health Care Authority.

Deb Wiser: Deb Wiser, Committee Member.

* For copies of the official audio taped record of this meeting, please contact Regina Chacon at (206)521-2027 pdp@hca.wa.gov.

Christine Klingel: Christine Klingel, Committee Member.

Susan Rowe: Susan Rowe, Committee Member.

Vyn Reese: Vyn Reese, Chair.

Carol Cordy: Carol Cordy, Vice Chair.

Barak Gaster: Barak Gaster, Committee Member.

Jason Iltz: Jason Iltz, Committee Member.

Regina Chacon: Regina Chacon, Health Care Authority.

Leta Evaskus: Leta Evaskus, Health Care Authority.

Donna Sullivan: Donna Sullivan with the Medicaid Purchasing Administration and Health Care Authority.

Duane Thurman: Duane Thurman, Health Care Authority.

Jeff Thompson: Jeff Thompson, Medicaid and Health Care Authority.

Thad Mick: Thad Mick, [inaudible].

Vyn Reese: Okay. Thank you. This is Dr. Reese and I want to open the meeting now with a discussion about selection of Chair and Vice Chair for the future. My term of office is up in January. So after the December meeting I will not be eligible to be Chair. So we need to discuss that. Carol has another year on her term. So she could be the Vice Chair for one more year. But we do need to select a Chair for certain today. And so I'm interested in your thoughts. No thoughts?

Jeff Graham: Vyn, this is Jeff Graham. The other person who's here today whose term is ending in December is Jason Iltz. And I don't think Alvin… is Alvin going to… if he's here today…

Woman: He'll be here for the afternoon portion of the meeting.

Jeff Graham: Yeah, okay.

Vyn Reese: So Jason is going to be gone.

Alvin Goo: So will I.

Vyn Reese: Alvin is going to be gone. Patti Varley is going to be gone.

Jeff Graham: No, Patti has one more year.

Vyn Reese: Oh, she has one more year. Okay. Patti has got one more year. Okay. Carol has got one more year. So it would need to be somebody who has more than one year to be chair. So that would be one of the qualifications.

Jeff Graham: That's true. The terms are two-year terms.

Vyn Reese: Right. So I'd like to nominate Barak Gaster.

Jason Iltz: This is Jason. I'll second that.

Vyn Reese: All those in favor say, "Aye."

Group: Aye.

Vyn Reese: Those opposed same sign? Barak is Chair.

Jason Iltz: This is Jason. I guess it should be noted Barak did accept the nomination. It was a little bit of a sideline conversation here, but he did accept that.

Vyn Reese: Exactly. In the hallway, but it actually already says Chair on your nametag there, Barak. But you have to wait another couple of months.

Barak Gaster: Thank you.

Vyn Reese: Now Vice Chair. Carol has agreed to serve for one more year as Vice Chair. And so that will end our discussion of that issue. Do we have someone online for the next drug class review? Are they ready to go?

Jeff Graham: I think we gave more time. Oh, Duane has a…

Duane Thurman: This is Duane Thurman. I've got a general announcement that went out to stakeholders. CMS has been delayed in publishing the 2010 rebate amounts and it's a result of health care reform. I think everyone knows about the budget situations coming up. So we're moving into very uncertain time in terms of what the Preferred Drug List or the Medicaid program will look like. And so the announcement says basically that the P&T Committee's work will be unchanged. But that we have frozen the Preferred Drug List as of our last… the first quarter of this year, April 2010, and we will not be doing the underlying cost analysis. So this will affect the meetings for today, December and February and then at the April meeting next year we're going to start doing… back to our normal procedures depending on what happens during the legislative session. And so the only changes that will be made to the Preferred Drug List during that list would be based on safety concerns, changes in the evidence, clinical concerns and so really nothing changes about your jobs. It's just that we will not be doing the underlying cost analysis or accepting supplemental rebates for that. So we'll see how… we'll keep you updated on what goes on during session.

Vyn Reese: So Dr. Thurman, if I understand this correctly we… if we make a decision today to add something to the PDL it wouldn't be added until after next year, after this is clarified. Is that right?

Duane Thurman: No. It… well, if you have a new drug that comes on and you say it needs to be preferred we will put it on, you know, saying that that's what the evidence and the clinical background requires. But we would not do it on the basis of, you know, where you're telling us that they are equally safe and effective. We will not be doing a cost analysis to determine which of those two competing drugs we would take.

Vyn Reese: I see. Okay.

Duane Thurman: Awkward times.

Vyn Reese: They are. And the Medicaid drug budget is in question too, totally, as I understand it.

Duane Thurman: Yeah. I hate to say it out loud but the current plan for the across-the-board cuts eliminates the adult pharmacy program for Medicaid effective March 1st of 2011. And so we, you know, the next step is the governor will be working on her supplemental budget, which gives the legislature and the governor more discretion. But we haven't seen anything on that and we really hit the wall in terms of where this money is going to come from. So the session starts the second or third week of January. My understanding is there needs to be some plan by February 1st or we have a whole new world.

Vyn Reese: It will be a booming business in the prisons and Western State.

Duane Thurman: I'm going to open an ER.

Jeff Graham: Dr. Reese, this is Jeff Graham, and I want to reiterate that if there's a safety issue that we would also take action on that—either a new drug that had to be there or if there is a safety issue on a present drug.

Vyn Reese: Okay. Great. So is Marian ready?

Jeff Graham: I didn't hear. We actually thought this would take a little bit longer. So she may not be calling in for a few minutes. Let me give her a call and see if she can call in.

Vyn Reese: Okay.

Jeff Graham: She's calling in.

Vyn Reese: Hi. This is Dr. Reese. Is that you, Marian?

Marian McDonagh: This is Marian.

Vyn Reese: Okay. We are um… we have your slides up and we're ready to go.

Marian McDonagh: All right. Great. Well let me get started then. So this is our third update on the atypical antipsychotic class and so you've definitely heard me go through this presentation in the past. I planned today to go through things primarily where there's new evidence that's meaningful. I'll be going through some of these sections where there really isn't much of anything new pretty quickly. But, you know, feel free to just interrupt me if you want to talk about any of the things as we go along.

So if we go to… let's see, the second slide. You'll see that for this update there are some new populations added. For schizophrenia we added adolescents. For bipolar disorder we added children and we added major depressive disorder in adults. So those are some fairly big new populations in this report. At least the bipolar disease in children and the major depressive disorder in adults that was… turned out to be fairly large. Now on the next slide, slide 3, are the drugs.

And um we have some new drugs as you know added to this update – asenapine, which is Saphris; iloperidone, which is Fanapt; and then paliperidone, which is Invega were the three new drugs. So a lot of the new evidence is about those, but we also have quite a lot of new evidence for what are now older atypical antipsychotics. So if we go to the next slide.

This is just the overview of what's included in the report and how many new studies were added for this update.

Slide 5 is the introduction for the beginning of the fairly large section on patients with schizophrenia.

So slide 6 is a summary of the entire evidence base for patients with schizophrenia. For the atypical antipsychotic drugs there are a lot of direct head-to-head trials in this population, which is great. You'll see in some of the others that there are very few, if any, head-to-head trials. We also include a large number of observational studies trying to look for important, meaningful, effectiveness outcomes. So things that would be seen long-term that patients care about. We still find, however, that a large percentage of those studies are poor quality.

So on slide 7 is the summary of the CATIE trial phases—all phases have been completed now and have at least primary publications. The only one that is new for this update is Phase III, which was basically a phase when patients could elect to enroll in another phase after discontinuing Phase II and then they would be randomized to one of nine open label treatments.

Now slide 8 is the first effectiveness outcome measure, which was looking at the risk of suicide or suicidal behavior and we did not have any new evidence here.

On slide 9 continuing with looking for effectiveness outcomes, for the risk of hospitalization we do have some new evidence. Again, it is still indicating that there's a lower risk of re-hospitalization with olanzapine, but the new evidence is consistent with the previous evidence. The last phase of CATIE, the Phase III, no differences were found between all the nine different arms there. But it prob- may be because they were not all that large.

Now if we go to slide 10 the new evidence we have here is under the heading of social function or social functioning. We didn't find… so in the study differences were not found between olanzapine, risperidone, quetiapine or ziprasidone and these were looking at measures of employment or general function outcomes. And these were generally health report or using scales to measure those outcomes.

On slide 11 looking at rates of discontinuation of the drug this, as you may remember, was the primary outcome measure for the CATIE trial and we had done a network meta analysis in the past and we re-ran that meta analysis with the new evidence adding in evidence for all of the new drugs. We also added another term in the analysis to adjust for duration of study. So we still find olanzapine has a lower rate of drug discontinuation and if you look on the next slide, the table shows you the odds ratios for these findings. So I'll continue on with this slide. If you want to you can refer to the numbers on the next slide. So olanzapine has a lower rate of drug discontinuation compared with aripiprazole and now we have asenapine and iloperidone added to the list. The list

includes quetiapine, risperidone and ziprasidone. There was no difference, again, between olanzapine and clozapine. Clozapine does have a lower rate of drug discontinuation than quetiapine, risperidone, ziprasidone and now iloperidone. So we didn't find differences among any of the drugs compared to paliperidone and it may be there are very few data entered into the analysis for this particular outcome measure for paliperidone. So it's not clear if we add more data if that would remain the same.

Okay. On the table on the next slide the highlighted bolded numbers are the ones that are statistically significant and all the rest are non-significant.

So moving on to slide 13 then looking at efficacy moving down the list of outcomes measures and moving into efficacy outcomes um we have some new evidence here but… consistent differences in efficacy are still not found between most of the drugs. There are a few exceptions. The pooled… a pooled analysis indicates olanzapine has a higher likelihood of response compared with aripiprazole, but the relative risk is 1.11. So the difference is rather small. Evidence of comparative efficacy is very limited for some of the newer drugs including asenapine, iloperidone and the extended release formulation of quetiapine. So I'll run through these just briefly. Olanzapine was superior to asenapine based upon improvement in the PAN scale, the positive and negative symptom scale. Quetiapine extended release was superior to quetiapine immediate release, again based on the PAN. In teenagers quetiapine was not found superior to placebo in overall response rates, but it was superior, again, based on changes, improvement, in the PAN scale. And then evidence for iloperidone was insufficient to make conclusions because it is… we only currently have placebo-controlled trials of iloperidone, so no direct evidence is available.

Now on the next slide, slide 14, looking specifically at the population who are having their first episode of schizophrenia symptoms um new evidence here is pretty limited. It's looking at olanzapine versus quetiapine. They were found similar to each in a small study of teenagers. We had been hoping that the European first episodes schizophrenia trial would be very helpful—it's larger, it's directly

comparing the drugs. However, when the study was published the analysis was in fact not comparative. We can just look indirectly at the numbers and see that quetiapine, olanzapine and risperidone look similar.

On the next slide moving on to the adverse events for patients with schizophrenia looking at again that primary outcome measure of discontinuation this time due to adverse events we again had done a mixed treatment comparison or network meta analysis and controlling for the differences in dose comparisons within the studies that may have existed and then study duration um, again we find differences are not… not clear among the other drug… sorry, among most of the drug comparisons. Um but the big one is, of course, that clozapine does seem to have a higher discontinuation rate due to adverse events compared with olanzapine, quetiapine and risperidone. We really don't have a lot of new evidence… new data added to the meta analysis for asenapine, iloperidone and paliperidone. So while those… on the next slide you'll see the odds ratios for those discontinuation rates. They may change as we add more data to the meta analysis in the future.

So on slide 16 you'll see the table with the odds ratios for discontinuation, the risk of discontinuation for adverse events and the three bolded numbers are the comparisons to clozapine where clozapine had a higher rate of discontinuation.

Now on slide 17 moving into the extrapyramidal symptoms new evidence here for asenapine indicates that it was consistently associated with higher rates or worse severity of extrapyramidal symptoms and most commonly that was akathisia compared with olanzapine. That's based on five studies.

Now looking at weight gain on slide 18, weight gain with olanzapine compared to risperidone, we've updated that meta analysis and find that in the short term trials the difference is 2.8 kilos. So patients on olanzapine gaining 2.8 kilograms more compared to those on risperidone. The observational evidence, which is generally longer term but also is probably… includes a broader… a types of patients and um also may include other cointerventions. The weight gain difference was smaller,

1.4 kilograms. So moving down the slide a little bit there, the… in patients with first episode schizophrenia this is where you see the weight gain difference between olanzapine and risperidone to be much better. So 5.26 kilograms difference. The weight gain between olanzapine and quetiapine the difference is similar to what we saw compared to risperidone 2.15 kilos difference in an odds ratio of 1.46 when looking at the risk of significant weight gain, clinically important weight gain. So weight gain evidence for the newer drugs is not comparative and so that's a real problem. You can't really… it's very difficult to make comparisons across these. We find very limited evidence for weight gain for the newest drugs, asenapine, paliperidone and iloperidone.

Now on the next slide looking at serum lipids we do not have any new evidence that was comparative. So the conclusions there are not changed.

Slide 20 – here we had very, very little new evidence as well. We had one new study that included paliperidone that found that the risk of sexual dysfunction was not different between risperidone and paliperidone. Again, those are very small and short-term studies.

Slide 21 was trying to look at subgroups here and trying to figure out if we can identify differences based on specific subgroups of the population for either benefits or harms. There are some hints but not enough comparative data to make any clear conclusions. For age, for example, the evidence we mentioned earlier among teenagers with schizophrenia quetiapine was not found superior to placebo based on response rates although it was superior based on improvements in the symptom scales. And then down at the bottom… the rest of the evidence here is really just placebo-controlled and not very helpful. But the disease characteristics one I do want to point out to you because the very first bullet is in patients with schizoaffective disorder. We really have very, very little evidence on patients with schizoaffective disorder. Many of the trials include a very… a small proportion, maybe anywhere from, you know, 5% to 10% with schizoaffective disorder. But the results are now stratified. So here we have a study done entirely in schizoaffective disorder patients. Aripiprazole and paliperidone were both found superior to placebo in these studies and in improvement of symptoms. And then

similarly paliperidone was found to be superior to placebo in improvements on mania and depression scores in patients who had those symptoms at baseline.

That completes the discussion of the evidence in patients with schizophrenia. I'm going to move on to the patients with bipolar disorder now. We will be getting back to serious harms looking across populations later in the presentation. So there's more evidence that includes patients with all of these different diseases for harms.

So looking at bipolar disorder in adults, the slide on 22, we'll get to the separate body of evidence in children in a little bit.

So moving to slide 23 this is the overview of the evidence. Again, the underlined evidence is what's new for this update. I should have said that earlier. So you can see on here that the only new head-to-head trial… or evidence is asenapine versus olanzapine, two trials. And then we have some indirect evidence in placebo-controlled trials that have been added for various drugs as well. And we didn't have any paliperidone studies that were able to be included due to our inclusion criteria.

So if we go to the next slide, slide 24, looking at effectiveness outcomes, here we're looking at the risk of hospitalizations. Unfortunately, we did not have any trials here. So we're looking at observational studies only. And here the risk with risperidone was higher than the risk… than the rate with olanzapine. And that was statistically significant. That's with monotherapy. With aripiprazole the risk was higher in adjunctive therapy with aripiprazole. That is was higher in comparison with ziprasidone, quetiapine, olanzapine and risperidone. Again, from observational evidence. Looking down at quality of life we had some new evidence here with olanzapine compared to asenapine where there was no difference found between the drugs.

Okay. On the next slide, slide 25; looking at remission rates, direct evidence indicates that remission is not different between olanzapine and risperidone or between asenapine and olanzapine. Then we have some indirect evidence on the slide as well and all of the drugs appear to

be superior to placebo in remission rates and the new evidence is underlined there with quetiapine extended release and aripiprazole.

On slide 26 looking at remission of acute depressive episodes we only have placebo-controlled trials here and all of the drugs were found to be superior to placebo. This time the new evidence includes quetiapine extended release.

Slide 27 is looking at acute treatment of rapid cycling and we did not find any new evidence for that particular population.

So looking at slide 28 we're still looking at the treatment of bipolar disease, bipolar disorder in adult patients and this is looking at maintenance. So based on indirect evidence only for a manic and mixed episode aripiprazole, olanzapine and quetiapine immediate release were all superior to placebo for monotherapy. With adjunctive therapy comparisons to placebo the time to recurrent was greater with quetiapine immediate release and long acting risperidone injection compared to placebo. So that's new evidence there. Looking at patients with depressed episodes there was a longer time to recurrence with quetiapine immediate release compared to placebo and for rapid cycling. The subgroup analysis in this study found a longer time to relapse with aripiprazole compared to placebo. So again indirect evidence only.

So now looking at harms on slide 29 looking at direct comparative evidence um adverse events looking at discontinuations due to adverse events, there were higher rates of discontinuation. So it's asenapine compared to olanzapine based on two trials with a pooled relative risk of 2.56. Looking at weight gain here we have… it looks similar to the findings we saw with patients with schizophrenia with olanzapine having a higher weight gain in comparison to other drugs. In this case the new evidence shows olanzapine compared with asenapine and the difference is 2.2 kilograms. Looking at extrapyramidal symptoms, differences were not found between olanzapine and risperidone or olanzapine and asenapine. Now that finding… no difference between olanzapine and asenapine is different to what we saw in the schizophrenia population where we did see a significant difference with a higher rate with

asenapine. This is based… this evidence is based on a single study here whereas the evidence in schizophrenia was based on five studies.

Looking on the next slide, looking at, again, indirect evidence, treatment-emergent mania in bipolar depression. This is a concern with many of the other drug classes that are used to treat depression… bipolar depression. Here the atypical antipsychotics did not find an increase in treatment-emergent mania with any of the drugs studied.

Now looking on slide 31, again, trying to examine the subgroups to see if we could find any evidence of a difference in a particular group, here the direct evidence looking at stimulants… patients who had co-occurring stimulant dependence there was no difference between quetiapine and risperidone on their mania rating scale scores. So the stimulant dependents did not affect the results. Now looking at demographics the evidence is not comparative. It's placebo-controlled, but the… no effects were seen looking at age, gender or race.

Now on slide 32 we're moving into the evidence for children and teens with bipolar disorder.

So on slide 33 the summary of the evidence. We have one head-to-head trial in preschool age children comparing olanzapine and risperidone and then we have some indirect evidence for placebo-controlled trials.

So looking on slide 34 looking at effectiveness outcomes the only one that we could identify in this evidence was quality of life and here there was no significant difference between aripiprazole and placebo, which is unusual. Usually you do see some difference between drug interventions and placebo on quality of life.

Moving to slide 35 looking now at efficacy outcomes in children with bipolar disorder. The direct evidence comes from a small study, 31 preschool age children. Here there is no difference in response based on improvement on the young mania rating scale or clinical global impression scale. But again this could change. You can see that the difference between 53% and 69%. If it was a larger study the [inaudible] statistically significant difference may have been found. For indirect

evidence for children and adolescents with manic and mixed episodes the drugs were all found superior to placebo. However, in teenagers with depressed episodes quetiapine immediate release was not found superior to placebo. And that was all monotherapy. Looking at adjunctive therapy quetiapine immediate release plus divalproex was found very similar to divalproex alone.

Okay. So moving to slide 36 looking at harms in children with bipolar disorder the weight gain here looking at the direct evidence again that small study in preschoolers, the difference was again not statistically significant. The difference… the absolute difference is about 1 kilogram. So again a larger study may find a statistically significant difference. That study was an eight-week study. So we're looking at the weight gain over eight weeks. Indirect evidence in children and teens, again, finds olanzapine to have the highest increase in weight relative to the other drugs.

On slide 37 looking at extrapyramidal symptoms again no difference was found between risperidone and olanzapine in that small study of preschool age children. Indirect comparisons compared with placebo there was a significant increase in EPS with aripiprazole and risperidone. The relative risk with aripiprazole being quite high, almost 7.

Now in moving on to the next population, the next group of studies is in patients with major depressive disorder on slide 38.

Slide 39 is the overview of the body of evidence. Here we found no direct head-to-head trials. We do have two observational studies looking at harms. Indirect evidence from placebo-controlled trials there's quite a bit. So looking at acute treatment we have… there's a group of studies with patients who have a history of inadequate response to antidepressants and most of that evidence is in adjunctive treatment adding the atypical antipsychotic to an antidepressant with only one monotherapy study. And then there's a smaller group of studies with patients who have no history of inadequate response, again, with a few studies with adjunctive treatment and five studies of quetiapine extended release monotherapy. There are also some maintenance treatment studies with adjunctive risperidone and treatment resistant

and quetiapine extended release monotherapy in patients with no history of treatment resistance.

Okay. So moving to slide 40 looking at all of the effectiveness outcomes that we could identify and again these are based on indirect evidence placebo-controlled trials only. So for suicidal ideation the atypical antipsychotics had no effect compared to placebo and that was adjunctive therapy with aripiprazole, adjunctive risperidone or monotherapy with quetiapine extended release. Functional capacity was improved adjunctive aripiprazole and adjunctive risperidone. Quality of life compared to placebo, the combination of olanzapine and fluoxetine and then adjunctive risperidone, quetiapine extended release monotherapy and in older patients all of those studies showed an improvement in quality of life compared to placebo. For relapse prevention fewer relapses were seen with the quetiapine extended release monotherapy in a study of 52 weeks.

On slide 41 looking at remission compared to placebo the drugs were found to have higher remission rates although the definitions of remission did vary and the pooled rates of remission are listed in the table. And the drugs there included here are risperidone, aripiprazole, olanzapine and quetiapine extended release. Most of those are adjunctive therapy studies.

So now looking on slide 42 moving into the harms for patients with major depressive disorder with weight gain we do have these comparative observational studies. It was… most of this evidence is coming from a small study, 100 patients who were inpatients the entire time. So it's a little bit different than what the kind of evidence we've looked at before for patients with schizophrenia. The mean weight gain with olanzapine plus SSRI was 4.21 kilograms, which was greater than was seen with quetiapine or risperidone, which were 2.89 and 2.40. So approximately 1.3 to 1.8 kilogram difference between the groups. Looking at indirect evidence weight gain was highest with olanzapine in these studies and lowest was quetiapine.

Now moving to slide 43 looking at extrapyramidal symptoms in patients with major depressive disorder. Again, looking at indirect evidence.

Adjunctive aripiprazole was the only atypical that was found to have a significantly increased risk of akathisia compared to placebo with the difference being 20%... 20% difference in the rates. Again, it's not head-to-head evidence compared to another atypical antipsychotic.

Looking at slide 44 examining the subgroup evidence. Here we do find some differences. So for demographics looking at gender, and again this is compared only to placebo, symptom improvement was greater for women but not for women with adjunctive aripiprazole. But with age there were no differences seen in the subgroup examinations of younger patients compared to older patients for aripiprazole, quetiapine XR and risperidone.

So moving on to the next population is on slide 45. Patients with behavioral and psychological symptoms of dementia.

On slide 46 you'll see here that we have very, very little new evidence here. So I'm going to skip… so you see that the only underlined is one interim study of intramuscular aripiprazole for acute agitation. And an additional study of aripiprazole oral added above there too. So I'm going to skip. Let's go… the next slides are all unchanged. Let's go to slide 50.

So this is looking at indirect evidence. So placebo-controlled trials with oral aripiprazole and here aripiprazole compared to placebo there is no statistically significant difference looking at efficacy outcomes. For the intramuscular aripiprazole, again, compared to placebo it was… it did find superior efficacy looking at acute agitation; so improving acute agitation.

All right. And on the next slide, slide 51 is the evidence on adverse effects and there was no new evidence provided by those studies.

So now we move on to the next population, slide 52, which is looking at children with pervasive development disorders or disruptive behavior disorders.

So on slide 53 for children with PDD there were two new trials of aripiprazole that focused on irritability. That's the new evidence here.

So on the next slide, slide 54, is the findings. Aripiprazole and risperidone both improved irritability symptoms in comparison to placebo.

So then slide 55 is looking at comparisons to haloperidol. There were no new studies here.

If we move to slide 56, this is looking at the evidence for efficacy in children with disruptive behavior disorders. Here we have only one new study in teenagers. It's a placebo-controlled trial of quetiapine. Quetiapine was found to have better improvement in efficacy than placebo looking at aggressive behavior outcomes. But not all of the outcome measures they studied were improved. This was a very small study as you can see, only 19 patients. So a larger study might show bigger differences.

So then looking on slide 57, looking at tolerability or adverse events in children with either PDD or disruptive behavior disorder. Here we have new evidence, again, only on aripiprazole and this is looking at weight gain. So the weight gain was greater with aripiprazole than placebo and the range of weight gain was 1.3 to 1.5 kilograms compared to 0.3 in the placebo group.

Okay. So now moving to slide 58 where we review the evidence on serious harms and this includes evidence across all the populations. However, most of the studies include the predominant… patients are… patients with schizophrenia.

So looking at the first slide in this section, 59, is looking at mortality. This time we have some new observational studies. So we have a total of 10. But it is… even with 10 observational studies it provides limited evidence because most of these studies are looking at the atypicals as a group compared to the older drugs, the conventional antipsychotics. So for all cause mortality the comparative evidence wasn't adequate to make conclusions about differences among the atypicals. There does seem to be an increased risk with specifically olanzapine, quetiapine and… sorry, that should say risperidone compared with conventional antipsychotics and still the evidence does indicate a reduced risk with clozapine compared to the conventional antipsychotics. Looking at sudden death

there's evidence that indicates a greater risk with atypical antipsychotics compared to no antipsychotics. There may be a dose response effect within this evidence. It's not entirely clear. A difference between the drugs was not clear and again it's because the studies are not really designed to ask that question. So for elderly patients the current studies do not find a difference in the risk for mortality among… or between the atypicals. But the newer drugs are not included in these studies. The risk with atypical antipsychotics as a group may be lower in older patients compared to the conventional antipsychotics.

Now slide 60 is looking at cerebrovascular events and here there is no new evidence.

Now looking on slide 61, cardiovascular and cardiac effects the only new evidence that we were able to add was a study using the Framingham Risk Score, it's a model. So adding that… using the evidence from the CATIE trial, running that through the Framingham Risk Score they came up with an estimate of 10-year risk of coronary heart disease with olanzapine to be increased by .5% whereas with risperidone decreased 5.6%. So it's a statistically significant difference there. They also found that the highest increase in risk was among those who had the highest baseline scores—the highest risk at baseline.

On slide 62 examining the evidence for the risk of new onset diabetes the increased risks with olanzapine compared to risperidone is still… the conclusion we now have six studies. The pooled odds ratio is 1.16. So it's a small increase in risk, but statistically significant. Limited evidence does not support an increase in risk with clozapine or quetiapine when compared to each other or with risperidone or olanzapine. And evidence on the risk with asenapine, iloperidone, paliperidone, ziprasidone or aripiprazole was just not found. We can't really do any estimates.

So on slide 63 though for tardive dyskinesia we do have some new comparative evidence. Previously this was an area that there was great concern but very little evidence. So here we have something that we… new to say. The comparative observational studies, there are two studies, suggest a significantly increased risk of new onset tardive dyskinesia with risperidone compared to olanzapine. These two studies,

six months and 36 months, so in the six-month study the incidents was 1% with olanzapine, 2% with quetiapine and 3% with risperidone. But the difference between olanzapine and risperidone was the only one that was statistically significant. In the longer study the rates are slight… just a little bit higher – 1.7% for olanzapine, 2.7% for quetiapine and 1.3 for um, I'm sorry, quetiapine and 3.3% for clozapine. The 36-month relative odds, so the odds ratio is risperidone versus olanzapine is 1.7. So statistically a significant increase in risk.

So looking at the next slide is trying to look at a variety of other harms. And here there's really nothing new. The seizure rate was changed just slightly by adding a single new study. Seizure rate that is associated with clozapine.

Okay. So then slide 65 is a summary. There's a lot of evidence to summarize in a single slide. So this is just some of the highlights. So I'm going to stop there and see if there are any questions.

Vyn Reese: Hi. This is Dr. Reese. I had one question. It's on slide 35. And it's the placebo response in depressed episodes of adolescents with bipolar disease and the placebo response was 67%. Is that correct? That's better than almost all of the drugs.

Marian McDonagh: Let me see where you are.

Vyn Reese: It's depressed episodes in adolescents.

Marian McDonagh: Oh yes. I know. No, you're absolutely right and that is what was reported. But it does seem very high and you'll see there that the quetiapine was 71 and there was no difference between the groups. So it does seem like something unusual was going on in that study and the placebo response rates in studies like this where, you know, the outcome measures are subjective is really a big issue right now because there are questions about have placebo response rates changed over time in those groups. So it's something that we could start looking at in this population here. But right now that's all I can tell you that really… that is what the study results showed.

Vyn Reese: It makes you wonder about correct diagnosis. In adolescents it can be difficult to diagnose.

Marian McDonagh: Okay. Well, that is a good point and I can make sure we look at that to make sure that that is emphasized in the report. You know, whether they… what did they do for… how did they diagnose the patients? That would be an important point.

Vyn Reese: Any other questions from the committee?

Barak Gaster: This is Barak. I had one question on slide 24 with hospitalization. I want to make sure I'm interpreting that correctly. Could you review that first bullet point?

Marian McDonagh: Okay. Let me get there. Okay. Go ahead.

Barak Gaster: So as far as adjunctive treatment aripiprazole compared with some of the others… the hospitalization rate was lowest for risperidone?

Marian McDonagh: So the hazard ratio that is shown there, the 1.5 for risperidone, is that where we're looking?

Barak Gaster: Exactly.

Marian McDonagh: Okay. So that is saying, "What is the rate of aripiprazole compared to risperidone over time?" And so the 1.5 is the increase with aripiprazole compared to risperidone. So you see that quetiapine also had a 1.5. So they are all very similar. The 1.5 to 1.7 for the other drugs.

Barak Gaster: Right. So the question is, "Is it worse or better?"

Marian McDonagh: Okay. So what it means is that aripiprazole is worse because it has a higher rate of hospitalization.

Barak Gaster: Thank you.

Marian McDonagh: Yep.

Patti Varley: This is Patti Varley and a question I have just overall is when I look at like this slide for instance in those comparisons there's really no specific dosage ranges looked at in any of these. Is there?

Marian McDonagh: No. You know, the dosage that are used in the studies are what we would put into… or what we would put into our analyses or what they have and I think that the reason we haven't pointed out doses is because they're very similar from study to study and we would point out if there are variations. So it's something that's unusual. I think the dose issue that we had in the past… so a few years ago in the schizophrenia population there were… some of the older studies had doses that were, you know, not comparable between the groups in a study or very big differences between studies and that's why in our network analysis we're putting in doses variable to control for confounding. But for these other newer studies we just don't see that as big of a problem. There's not variation like there used to be.

Patti Varley: Thanks.

Vyn Reese: Any other questions? Why don't you go ahead and go over the summary then.

Marian McDonagh: Okay. So on the summary slide, slide 65, we didn't find a lot of differences between the atypicals in short-term efficacy in patients with schizophrenia, bipolar disorder or dementia. Differences in most effectiveness outcomes were not clear and uncertainty still exists. So for example quality of life – there seems to be just a… few instances of a difference, but many of those are in non-comparative studies. So placebo-controlled trials. In patients with schizophrenia clozapine reduced suicides and suicidal behavior, but resulted in stopping the drug due to adverse events more often than the others. However, clozapine and olanzapine resulted in lower rates of discontinuation of drug for any reason over periods of up to two years. In adults with bipolar disorder asenapine resulted in a higher risk of stopping drug due to adverse events compared to olanzapine. Comparative evidence was not available for the use of the drugs in adults with major depressive disorder, children or adolescents with pervasive developmental disorders, or children with disruptive behavior disorders. Olanzapine resulted in greater weight gain

than the other drugs, 6 to 13 pounds or more on average and a 16% increase in risk of new onset diabetes while risperidone resulted in an increased risk of new onset tardive dyskinesia. While clozapine has been shown to be associated with an increased risk of seizures, agranulocytosis; among the other drugs serious harms have not been clearly shown. Evidence on long-term harms for the newest drugs is just… is lacking. Just we don't have it.

Vyn Reese: Okay. Thank you very much. Could you stay on the line while we have stakeholder input?

Marian McDonagh: Okay.

Vyn Reese: I want to remind stakeholders that you have three minutes to speak and that will be timed. The first stakeholder on the agenda is Dr. John Tran from Spokane Mental Health. On deck is Steve Cheng from Eli Lilly. Be certain to state whether you're recommending a drug company or yourself too.

John Tran: Okay. Hi. I'm Dr. John Tran from Spokane, Washington. Actually I'm coming by myself; representing the east side and just also some of the opinion from my colleagues over there. We really want to encourage open access for medications, especially for the newer atypical antipsychotics such as iloperidone and asenapine. I do have clinical experience using them and for example in iloperidone we… I… especially in my own patient population it seems to be helpful for the chronic schizophrenic patients. It seems like the long-term at least the metabolic… some of the metabolic side effects are better. And then on the other hand for asenapine that I think the mode of delivery is actually very novel in the sense that it absorbs through the mucosa… oral mucosa instead of having to swallow the medication orally. So I think that the [inaudible] also helpful for patient who tend to cheek their medication when we give it to them. So I think it's very important to keep those things in mind when we consider, you know, to be able to have access for these medications in case a Medicaid patient would need them. So thank you.

Vyn Reese: Any questions from the committee? Okay. Thank you. Next speaker is Steve Cheng, Eli Lilly. On deck is Helen Nilon, Mental Health Action.

Steve Cheng: Good morning. My name is Steven Cheng. I'm a Health Outcome Liaison with Eli Lilly and Company. Today I would like to speak on behalf of Zyprexa Relprevv long-acting injection. Zyprexa Relprevv was approved last December by the FDA for the treatment of schizophrenia in adults. It is a long-acting deep intramuscular injectable depot formulation of olanzapine different from the short-acting Zyprexa intramuscular. It is dosed every two to four weeks. Zyprexa Relprevv could serve as a viable treatment option for schizophrenia patients who have challenges number one, treating… staying adherent to daily oral medication, number two a history of previous schizophrenia episodes, and number three a patient with re-emerging schizophrenia symptoms. Short-term efficacy was established in an eight-week placebo-controlled trial in adult patients with schizophrenia. Total pan scores showed statistically significantly improvement from baseline to endpoint with each dose of Zyprexa Relprevv as compared to placebo.

A second longer term maintenance efficacy trial of 24 weeks in adult patients with schizophrenia showed Zyprexa Relprevv doses were each statistically significant superior to low dose Zyprexa Relprevv in time exacerbation of symptoms.

Regarding safety Zyprexa Relprevv was found to have a similar safety profile to oral olanzapine with the exception of injection-related events. This included post-injection delirium, sedation syndrome, or PDSS. PDSS events included a wide range of signs and symptoms of sedation from mild to moderate, severity to coma and our delirium including confusion, disorientation, agitation, anxiety or other cognitive impairment. Across all clinical trials PDSS events have occurred in less than .1% of injections and approximately 2% of patients. The potential for onset of PDSS event is greatest within the first hour after injection. The majority of cases have occurred within the first three hours. All patients largely recovered within 72 hours and the majority of these patients have chosen to continue treatment with Zyprexa relprevv.

Labeling for Zyprexa Relprevv includes a requirement for the patient to be observed at a healthcare facility with ready access to ER services for at least three hours following each injection and to be accompanied to his or her destination upon leaving the facility. Lilly worked with the FDA to develop a REMS program which includes a communication plan, a patient medication guide, and a mandatory patient care program. This restricts distribution of Zyprexa Relprevv to prescribers, healthcare facilities, pharmacy services and patients enrolled in the program. The goal of the patient program is to mitigate the risk of negative outcomes. We ask that you consider Zyprexa Relprevv as a treatment option for your schizophrenia patients who have challenges with treatment adherence. Thank you for your time.

Vyn Reese: Thank you. Questions? Okay. Thanks. Next up is Helen Nilon from Mental Health Action and on deck is Fred Amberger from Novartis.

Helen Nilon: Hi. My name is Helen Nilon. I'm here today as the Executive Director for Mental Health Action. I'm also speaking on behalf of the Community Transformation Partnership, which is an organization of organizations that includes 16 organizations such as NAMI of Washington, Passages, A Village Project II, Parents are Vital in Education, World Bridgers, Consumer Voices are Born, etc. We represent about 100,000 individuals that are your clients and you serve.

We are very concerned about what's going on. We know that we're in dire times. I think that there's probably one individual in the room who's ever lived through times that are serious as us here today. What we're concerned about is that adverse effects of the policies that you're making; the adverse consequences of having some of these drugs be for individuals. You're Generics First proposal where you have risperidone, which, you know, the evidence today showed how it's higher with tardive dyskinesia although anecdotally we know that far more than 4 out of 100 people that have been on risperidone talk about the symptoms that they've had. I mean most everybody I know who's been on it has talked about having adverse effects, including myself.

We're very concerned with the tardive dyskinesia that's reported. You do have studies that show that… and I don't know if I say the generic name

correctly, aripiprazole, that the quality of life with… I guess it's Abilify. The quality of life with that medication is far superior than the quality of life you can receive on a lot of these other medications specifically because of the side effects. And so if we're looking at individuals being okay with the level of their quality of life as we perceive it versus their self-report of what their quality of life, quality of life and I would hope that your indicators would show where are these people in work compared to the general population, compared to the overall average for people in the system? Also the short-term and long-term effects. When you have something like Abilify literally you know within a week in many, many cases whether or not that drug works for you. If it doesn't you can go on to something else versus something like risperidone and the other drugs that you're talking… we have to be on those drugs for months and months with severe side effects. We're talking about people who are sitting, shaking, drooling, unable to function in their life—that is no quality of life—while their bodies are getting used to these medications versus other drugs—the atypicals that are working on specific parts of your brain. They are not "buck shot" so to speak. They are working on specific neurotransmitters and receptors…

Jeff Graham: Please limit your remarks.

Helen Nilon: Yes. So in conclusion we would really like you to reconsider some of the policies that you're making today. They do have dire effects for many people.

Vyn Reese: Are there questions from the committee? I have one comment. I don't think the data supports that Abilify is the most effective drug with the least side effects.

Helen Nilon: No, I wasn't saying that.

Vyn Reese: So it's not…

Helen Nilon: I didn't mean to say that Abilify is the end all, beat all. I'm just pulling the one that I recognize the name. If you had any other brand names I don't recognize them. I happen to know that one.

Vyn Reese: Okay.

Helen Nilon: But I do know that it can go into effect in five to seven days and I'm talking from a deep suicidal depression that should be hospitalized in five days completely gone and has remained so for years.

Vyn Reese: Okay. Thank you. Any other questions from the committee? Thank you. Next person up is Dr. Fred Amberger from Novartis. On deck is Stephanie Kornechuk from Genoa.

Fred Amberger: Good morning. I'm Dr. Fred Amberger. I'm a Scientific Director with Novartis and I want to thank the committee for opportunities to make a few comments regarding Fanapt. Fanapt tablets are indicated for the acute treatment of schizophrenia in adults. The FDA approval of Fanapt was supported by two placebo and active controlled short term trials of four and six week's duration. Safety data was derived from more than 2,000 patients in short- and long-term studies. Both trials enrolled patients who met the DSM three and four criteria for schizophrenia. Fanapt was shown to be superior to placebo in controlling symptoms of schizophrenia using the pans and the BPRS scales. Efficacy was demonstrated across doses of 12 mg to 24 mg per day, which is the recommended daily target dose range. Fanapt must be titrated slowly from a low starting dose to avoid orthostatic hypertension. Titration to the lowest effective dose of 12 mg per day can be achieved in four days with the use of an available titration pack.

Fanapt should be given as a b.i.d. dose. The effectiveness of Fanapt for more than six weeks has not been systematically evaluated in clinical trials. Therefore, the physician who elects to use Fanapt for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient. The most common adverse events are dizziness, dry mouth, fatigue, nasal congestion, orthostatic hypertension, somnolence, tachycardia and weight gain. In clinical trials discontinuation rates due to side effects for patients on Fanapt and on placebo were similar. The incidents of akathisia, the feeling of inner restlessness often associated with other antipsychotics was also shown to be similar between placebo and Fanapt up to the maximum dosage range… or dose of 24 mg per day. 13% of patients taking Fanapt

experience a weight gain of 7% or more body weight in clinical trials. Across all short- and long-term studies the overall mean weight gain from baseline to the end of this trial was 2.1 kilograms. Additionally, patients did not experience medically important changes in triglycerides and total cholesterol levels. Fanapt also demonstrated a low incidence of extrapyramidal symptoms that were similar to placebo including Parkinsonism, dystonia, dyskinesia and bradykinesia.

Individuals with schizophrenia face enormous challenges. And while there's no cure it can be a manageable illness when a patient has the right medication. It's important to have a therapeutic option like Fanapt that can manage symptoms and enable functioning with a rate of akathisia no higher than placebo and without medically relevant changes in triglycerides and total cholesterol levels. Thank you for this opportunity. Do you have any questions or comments?

Vyn Reese: Any questions from the committee? Thank you.

Fred Amberger: Thank you.

Vyn Reese: Next is Stephanie Kornechuk from Genoa and on deck is Dr. Esther Estes from Merck.

Eleanor Owen: My name is Eleanor Owen and…

Jeff Graham: Eleanor, you're out of order right now. You will have a chance to speak, but the next person has already been called. Thanks.

Eleanor Owen: Sorry.

Vyn Reese: It's Stephanie Kornechuk.

Stephanie Kornechuk: Hi. My name is Stephanie Kornechuk. I'm a Pharmacist with Genoa Healthcare. We operate eight pharmacies in non-profit community mental health centers in Washington State. As our focus is on the mentally ill patient, we have hands-on practical experience helping these patients obtain access to the medications they require. Our pharmacists have daily interaction with some of the most severely mentally ill patients

in Washington's Medicaid program. We encourage our patients to be compliant and adherent and follow up with them when they are late for refill. We drive the paperwork process for prior authorizations, we track down insurance information, we walk them through obtaining patient assistance medication when they cannot afford medication.

We realize that the Medicaid program is facing a significant budget shortfall and are willing to work with the department to help minimize costs. We have already absorbed the AWP rollback of September 2009 and yet continue to provide the same high level of service to our Medicaid clients. There is no doubt that pharmacists are among the most easily accessible of all healthcare professionals and are dedicated to ensuring all patients have access to the right medication at the right time and the right dose.

In treating mental illness access to all of the available antipsychotic, antidepressant and mood stabilizing agents is critical to the treatment plan with the patient. A stable patient obviously requires less healthcare dollars than an unstable one. I think we observed that in the CATIE trial. It demonstrated 75% of participants discontinued taking their antipsychotic before the trial ended at 18 months. In fact, 50% of these patients were lost to follow-up. This demonstrates that even with extensive professional contact and intervention, non-compliance and non-adherence is extremely common among the schizophrenic patient population.

While we support the generics first program for antipsychotic prescribing in the newly diagnosed patient, medication choice for the treatment resistant patient needs to allow for open access to all available antipsychotics. I'd encourage you to consider the addition of Invega Sustenna to the Preferred Drug List and allow for its inclusion on the prior authorization list. Our experience with the current Provider One prior authorization process for Sustenna has been mixed. It is primarily dependent on the ability of the physician to correctly complete the paperwork process. We have seen some delays in treatment due to incomplete applications. This is especially difficult to manage when the patient has commenced therapy in the hospital and now requires their injection as an outpatient.

The frustration lies in the fact that the application process is out of our hands yet it is the pharmacist who must act as a liaison between the physician, Medicaid, nurse administering the medication and the patient waiting. Much time can be wasted in this process, which is inefficient and ineffective. We've also experienced a lack of notification by Medicaid once the prior authorization has been approved, which can lead to a delay in therapy.

We've yet to have a request for a prior authorization for Invega Sustenna denied, which indicates that it is being prescribed appropriately. Since Risperdal Consta is already a preferred medication, the addition of Invega Sustenna to the Preferred Drug List makes clinical sense, it is similarly priced to Risperdal Consta, is administered once every four weeks in the deltoid muscle and is very well tolerated. Thank you.

Vyn Reese: Thank you. Any questions from the committee? Okay. Next up is Dr. Esther Estes from Merck. On deck Kim Laubmeier from Bristol Myers Squibb.

Esther Estes: Hello. My name is Dr. Esther Estes. I'm a Regional Medical Director with Merck. I was formerly a practicing internist and I'm also board certified in preventive medicine. I am here today to provide information on a newer atypical antipsychotic – asenapine or Saphris is an atypical antipsychotic indicated for the treatment of schizophrenia. The efficacy of Saphris was established in two six-week trials and one maintenance trial in adults. It's also indicated for the acute treatment of manic of mixed episodes associated with bipolar one disorder. Efficacy was established in two three-week monotherapy trials in adults. It's also indicated as an adjunctive therapy with either lithium or Valproic for the acute treatment of manic or mixed episodes associated with bipolar one disorder. Efficacy was established in one three-week adjunctive trial in adults.

Saphris is a sublingual tablet and will dissolve in saliva within seconds. Patients should be instructed to not eat or drink for 10 minutes after administration. Saphris is not recommended in patients with severe hepatic impairment. Dosage adjustments are not routinely required on

the basis of age, gender, race or renal impairment status. The recommended starting dose for the treatment of schizophrenia or as an adjunct to lithium or Valproic in the treatment of bipolar mania in adults is 5 mg sublingual b.i.d. and the dose can be increased to 10 mg sublingual b.i.d. The recommended starting dose for bipolar one monotherapy is 10 mg sublingual b.i.d. The dose can be decreased to 5 mg b.i.d. if there are adverse events.

As with all atypical antipsychotics there is a black box warning that elderly patients with dementia related psychosis treated with antipsychotics are at increased risk of death. Saphris is not approved for the treatment of patients with dementia related psychosis.

The most common adverse reactions in schizophrenia were akathisia, oral hypoesthesia and somnolence. The safety profile of Saphris in the maintenance treatment of schizophrenia was similar to that seen with acute treatment.

The most common adverse reactions in bipolar one disorder were somnolence, dizziness, extrapyramidal symptoms other than akathisia, and weight increase. And during the adjunctive therapy trial in bipolar disorder were somnolence and oral hypoesthesia.

In a 52-week double blinded comparator controlled trial of patients with schizophrenia or schizoaffective disorder the mean weight gain from the baseline was 0.9 kilograms or 2 pounds. The proportion of patients with a greater than or equal to 7% of increase in body weight was 14.7% at endpoint. In the same 52-week trial the mean change from baseline for fasting glucose was an increase of 2.4 mg per deciliter. A decrease of 6 mg per deciliter for a total cholesterol. A decrease of 9.8 mg per deciliter for fasting triglycerides and increasing…

Jeff Graham: Please conclude your remarks.

Esther Estes: Okay. You may be wondering why another treatment from this class… schizophrenia and bipolar are severe mental disorders with significant disability. Unlike many other chronic diseases, lifestyle modification such as diet and exercise do little for these illnesses. Yes, several treatment

options do exist today and they have major impact on patient's lives and society. In the not-too-distant…

Jeff Graham: You need to conclude your remarks.

Esther Estes: Okay. I'm getting to that point now.

Jeff Graham: Why don't you say you're done?

Esther Estes: Okay. I just want to make one comment—one sentence. Scientific understanding of these disorders are still in their infancy. Despite the treatment options patients often relapse and require prolonged hospitalizations and depend on trial and error of various treatments. Truth is we do not know exactly how these treatments work. I cannot disagree with the generics first…

Jeff Graham: You have not concluded your remarks. Would you please turn off her microphone?

Vyn Reese: Okay. Thank you. Next up is Kim Laubmeier from Bristol Myers Squibb. On deck Laura Litzenberger from Janssen Pharmaceuticals.

Kim Laubmeier: Good morning. My name is Dr. Kim Laubmeier, Senior Medical Science Liaison for Bristol Myers Squibb. I'd like to thank you for this opportunity to provide testimony on Abilify or aripiprazole. The safety and efficacy of aripiprazole has been studied in multiple psychiatric diagnoses in both adult and pediatric patients. In the resulting 14 FDA approved indications can be summarized as follows: the treatment of schizophrenia in adults and adolescents age 13 to 17, acute and maintenance treatment of manic or mixed episodes associated with bipolar one disorder in adult and pediatric patients age 10 to 17, the use as adjunct therapy to antidepressants in adults with major depressive disorder who have shown an inadequate response to prior antidepressant therapy, the treatment of irritability associated with autistic disorder in pediatric patients age 6 to 17, and the IM formulation that's been indicated for acute agitation associated with schizophrenia or bipolar one disorder in adults.

According to surveillance data about 75% of aripiprazole prescriptions are for those approved indications and given that the DERP report so nicely summarized most of the registrational trial data I'm just going to focus my comments on a few Pharmacoeconomics studies. A retrospective cohort study was conducted in patients with bipolar one disorder using the Pharmetrics database. The study compared the rate of psychiatric hospitalization and inpatient costs when patients were treated with either aripiprazole, ziprasidone, olanzapine, quetiapine or risperidone. Aripiprazole was associated with a significantly lower rate of hospitalization and lower total psychiatric medical costs and monotherapy on any of the other atypicals. And I just want you to know that this is actually consistent with the UHC data that was highlighted today. The question around slide number 4, that data actually comes from the Kimminal(?) publication and I'd just like to read the results of that study.

Compared with aripiprazole all other atypical antipsychotics were associated with a significantly shorter time to hospitalization. So the advantage there was actually aripiprazole. Although the mechanism of action of aripiprazole is unknown it is proposed to be mediated through a combination of partial agonist activity at D2, D3 and 5HT1A receptors and antagonist activity at 5HT2A receptors. In fair balance I do call your attention to the two boxed warnings for aripiprazole—increased mortality in elderly patients with dementia related psychosis and suicidality in antidepressant drugs. In addition, I do have the full PI available for the committee. It's also available at abilify.com.

In closing, aripiprazole has a broad range of indications across adult and pediatric populations. As such, Bristol Myers Squibb notes [inaudible] America Pharmaceuticals respectfully asks that aripiprazole remain available as a first line agent and upon request I'm happy to answer any questions.

Vyn Reese: Any questions from the committee? Thank you. Next up is Laura Litzenberger and on deck is Lisa Trigg from Navos Mental Health.

Laura Litzenberger: Good morning. My name is Laura Litzenberger. I'm a Health Economics and Outcomes Research Liaison with Ortho-McNeil Janssen

Pharmaceutical. Earlier this year the committee heard data from a chart review of high cost Medicaid patients with schizophrenia and in that chart review there was evidence that a high degree of non-adherence was associated with these people's high cost.

The conclusion or one of the conclusions of that study was that long-acting therapies should be considered. Invega Sustenna is a long-acting atypical antipsychotic that's given in once-a-month injections. There's evidence that the drug starts working within four days of initiation of therapy. It's indicated for acute and maintenance therapy of adults with schizophrenia. We know that dosing these patients can be somewhat… there can be an issue with patients coming back in or compliance with these patients. With Invega Sustenna there's data to indicate that the monthly dose can be extended up to six weeks. So when a patient is not around to get that medication it's not as if you've lost that patient to therapy. So the monthly injection can be given at a six-week interval. And in fact we know that you can… patients can have a lapse in therapy of up to six months without re-initiating the first doses of Invega Sustenna. This is really important when patients are transitioning between the hospital and the mental health facilities, the community or changing within communities. These patients may not get back into therapy right away. So this extended period of time will allow those patients to continue therapy and getting the benefit from the medication.

There are recent data that suggest… that will be presented later this year that there is a decrease in hospitalizations associated with Invega Sustenna. And in our clinical trials of patients that were in our long-term maintenance therapy comparing the rate of hospitalization after they started on Invega Sustenna to the period of time before they started Invega Sustenna hospitalization rates were decreased from .35 to .04 hospitalizations per patient years.

Because of the uniqueness of Invega Sustenna and its benefits in patients with schizophrenia we'd like to ask the committee to add Invega Sustenna to the PDL.

Vyn Reese: Thank you. Any questions? Thanks. Next on deck… or next up is Lisa Trigg from Navos Mental Health and on deck is Suchetta Beheray, PharmD.

Lisa Trigg: Hi. My name is Lisa Trigg. I'm the Lead Psychiatric Nurse Practitioner for Navos Mental Health Solutions on the inpatient side. And I treat patients who are seriously mentally ill. My patient… 99% of my patients come to me as a result of being a danger to themselves, a danger to others or grave disability, and most of these hospitalizations are re-hospitalizations and they are admitted due to either non-adherence to their medications or treatment failure of their medications.

Long-acting agents are ideal for treating non-adherent patients, but the agents available in the generic realm have unfavorable side effects. For instance Haldol Dec can be very harsh with movement disorders prominent and patients frequently refuse to take further injections after they're discharged from the hospital where we can actually force them to take the medicine.

Risperidone is a good medication, but it requires two painful injections per month and takes up to three weeks for the first dose to be effective. I have been having a lot of success over the last year with Invega Sustenna. It requires one small deltoid injection per month after the initial loading dose and it's effective within the first few days of injection. Remarkably, I've had a half a dozen patients tell me that they really like their Invega Sustenna, which is really unusual. I had never had a patient tell me before that they liked their antipsychotic medication.

The second reason patients are admitted to my hospital are on grounds of danger to others, danger to self or grave disability, is the failure of the treatment that they're on. Perhaps they've been adherent, but the treatment fails anyway. Just this year I cared for two seriously mentally ill patients who were typically treatment adherent, but had terrible side effects to literally every medication available. I happened to use Fanapt with these two patients and they both resolved and were able to leave the hospital with good prospects for further adherence.

I think it's important to have a wide variety of medications available to treat thought and mood disorders because although the meds all do roughly the same thing, the people are different and have different reactions to these medications.

Also I'd like to say that at present the prior authorization process is onerous on prescribers like me and I typically have to send my prior authorizations with barcode coversheets three to four times to Provider One before they're approved for Invega Sustenna or Fanapt. This takes precious time away from my patient care.

I'd also like to point out a study that compared the outcomes of access to antipsychotic medications across Medicaid prescription drug policies and show that this study by West et al in 2009 showed that patients with medication access problems had 3 to 6 times greater likelihood of adverse events including emergency visits, hospitalizations, homelessness, suicidal ideation or behavior, or incarceration.

I'd like to ask you to consider…

Jeff Graham: Please conclude your remarks.

Lisa Trigg: Thank you for your time.

Vyn Reese: Okay. Thank you. Any questions from the committee? Okay. Next up is Suchetta Beheray and on deck is Elham Tabarski from AstraZeneca.

Suchetta Beheray: Good morning. My name is Suchetta Beheray and I'm a Pharmacist currently working at Community Psychiatric Clinic. CPC sees patients with mental illness in King County. As a CPC pharmacist I've had the fortune to interact and work with hundreds of patients with mental disorders predominantly schizophrenia and bipolar. I'm here today to advocate the need for open access to all atypical medications and particularly long-acting injectables like Invega Sustenna.

Because of the complex disease state it is very hard to use a cookie cutter approach to treat individuals. While genetics first may work for some individuals it doesn't work for all because of the complexity of the

disease. Granting open access to all medications lets the provider make the best clinical decision based on patient evaluation, medical history, psychoanalysis, symptoms and diagnosis.

Another major concern with mental illness is compliance. The [inaudible] compliance is at best marginal. Injectables come in handy to resolve the situation. They also help in reducing hospitalization. The current prior authorization process, the process with the new Provider One is very time consuming and imposes unnecessary [inaudible] in providing medications to patients. It has at times taken us up to three weeks to get a PA through, which is critical time lost in patient care. These patients are very vulnerable and can easily fall apart if they do not get their medications in a timely manner. Also if we do not provide them with meds when they are in the clinic they may not show up later.

Injectables are prescribed often not as a first option, but as an only option to stabilize a patient. Any delay in authorization process could be the difference between success and failure, independence versus hospitalizations, and also at times life versus death. And so I urge you to extend complete access to long-acting injectables like Sustenna. Sustenna also has a unique advantage that it's once a month and that helps with patient adherence and also acceptance.

Lastly, if we focus on cost analysis, Invega Sustenna's monthly treatment costs are the same as that of any other branded oral atypical antipsychotic and costs significantly less than hospitalizations and way less than non-compliance costs.

In my capacity as Clinical Pharmacist I've seen several patients decompensate due to multiple reasons including failed access to medications and formidable co-pays. But today I would like to share with you some success stories.

Have currently about 25 patients stabilized on Sustenna who have successfully managed to prevent hospitalizations, to have graduated from residential facilities and moved to independent housing. Another one was stabilized first on oral risperidone, lived in a residential facility but lost access to it, continued oral risperidone in an outpatient setting. It

was non-compliant and eventually got put on Invega Sustenna, which he has been receiving for about a year. The patient is now extremely stable, has a part-time job…

Jeff Graham: Please conclude your remarks.

Suchetta Beheray: …and has an insurance. So he's independent now. So I strongly request you to grant complete access to Invega Sustenna. Thank you.

Vyn Reese: Thank you. Questions? Next up is Elham Tabarsi from AstraZeneca. On deck Erica Horn Hero House.

Elham Tabarsi: Good morning. I'm Elham Tabarsi, a Senior Regional Scientific Manager for AstraZeneca Neurosciences. Thank you for the opportunity to speak to you today about Seroquel XR and Seroquel. Seroquel XR is FDA approved as adjunctive treatment to antidepressants in adults with major depressive disorder or MDD based on two six-week clinical trials in adults with MDD who had an inadequate response to antidepressant treatment.

Seroquel XR formulation releases drug predominantly while erosion control over a day.(?) Peak plasma levels are reached within six hours. It offers once-a-day dosing for all approved indications. Seroquel XR is the only medication in its class approved by the FDA to treat both MDD as adjunctive therapy in acute depressive episodes associated with bipolar disorder as monotherapy. Seroquel XR is also proved for the acute treatment of depressive episodes in bipolar disorder as monotherapy, acute manic or mixed episodes in bipolar one disorder as either monotherapy or adjunctive therapy to the [inaudible], for the maintenance treatment of bipolar one disorder as adjunctive therapy to [inaudible] and for the treatment of schizophrenia as monotherapy.

Seroquel the immediate release formulation is approved for the treatment of schizophrenia in adolescents 13 to 17 years old and for the acute treatment of manic episodes associated with bipolar one disorder in children adolescents 10 to 17 years old. Seroquel is also approved in adults for the acute treatment of depressive episodes associated with bipolar disorder, acute treatment of manic episodes associated with bipolar one disorder both as monotherapy and as adjunct therapy to

[inaudible] for the maintenance treatment of bipolar one disorder as adjunctive therapy to lithium or [inaudible] and for the treatment of schizophrenia.

Prescribing information for Seroquel XR and Seroquel contain the following box warnings: elderly patients with dementia related psychosis treated with atypical antipsychotic drugs are at increased risk of death compared to placebo. Seroquel XR and Seroquel are not approved for the treatment of patients [inaudible] related psychosis. Antidepressants increase the risk of suicidal thinking and behavior in short-term studies in children, adolescents and young adults with major depressive disorder, and other psychiatric disorders. Seroquel is not approved for use in patients under 10 years of age, and Seroquel XR is not approved for use in patients under 18 years of age.

Prescribing information for Seroquel and Seroquel XR include warnings and precautions for neuroleptic malignant syndrome, hyperglycemia and diabetes, hyperlipidemia, weight gain, tardive dyskinesia, orthostatic hypertension, leucopenia, neutropenia and [inaudible], risk of cataracts, seizures, hypothyroidism, hyperprolactinemia, [inaudible] elevations, potential for cognitive and motor impairment, [inaudible] body temperature dysregulation, dysphasia, suicide, QT prolongation, [inaudible] withdrawal. Prescribing information also includes a warning and precaution regarding an increase in blood pressure in children and adolescents. Most commonly observed adverse reactions in adults were insomnia, dry mouth, dizziness, constipation, increased appetite, [inaudible] abdominal pain, postural hypertension, [inaudible], weight gain, fatigue…

Jeff Graham: Please conclude your remarks.

Elham Tabarsi: Thank you very much for your attention. Are there any questions regarding Seroquel XR and Seroquel? And I would refer you to the prescribing information for the full listing of adverse events.

Vyn Reese: Any questions? Thank you.

Elham Tabarsi: Thank you.

Vyn Reese: Next up is Erica Horn from Hero House and on deck is Eleanor Owen from NAMI.

Erica Horn: Good morning. On behalf of Hero House and the Washington State Clubhouse Coalition, which is a statewide coalition of consumer run, consumer driven services. We have historically disagreed with the generics first policy, which will be discussed later today. However, we understand that the committee is going forward and therefore oppose the associated barriers with the access. For those of us in the business of providing community outpatient services to the people referenced in the trials, which were reviewed by the committee earlier today, we know that the trust between the patient consumer and the doctor is invaluable in the long-term treatment and management of mental illness. The barriers associated with access rules interrupts this trust thus extending the community based services needed to support the consumer. Thank you for your time.

Vyn Reese: Questions? Okay. Thank you. And the last stakeholder is Eleanor Owen from NAMI.

Eleanor Owen: Thank you very much. I wish first to thank the committee for its efforts in attempting to objectively analyze what would be the most cost-effective, the most efficient medication for individuals with major mental illnesses. Secondly, I would like to also comment on the need for this committee to somehow or other develop an abstract such that this information can be broadly distributed. There are 167,000 individuals with mental illness enrolled in the publicly funded system in Washington State. This valuable information probably only goes to 1,000 people… 2,000 people… 3,000 people and I honestly believe that if we could get this information to the individuals who are most impacted by it this committee would be doing an invaluable service.

I also wish to say that what I missed in the analysis was a clear recognition that the research was based upon comparable doses. In the 30 odd years that I have been involved my observation—indirect observation has been that the dosage is critical in whether or not the

person's quality of life and the effectiveness of that medication is significant. Thank you very much.

Vyn Reese: Thank you. Any questions?

Duane Thurman: Duane Thurman. I just want to make one point of clarification. In the remarks that we've heard about, the generics first initiatives and all of that, I'd like to point out that that really is a function of the Drug Utilization Review Committee and in fact this afternoon Dr. Thompson will be presenting about adult atypicals and I want to make it very clear that the role of the P&T Committee is not to make any cost-effectiveness arguments or to consider any of the evidence of cost and that was part of the reason I was explaining that we're not doing that portion for a couple of meetings, but your role stays the same. You're looking at the evidence objectively and telling us whether there are significant differences, drugs that we need to include, drugs that have significant safety or special effects in populations. So I just want to make that clear that we still have a dual role and I want to make clear that we are not considering cost or cost-effectiveness in this discussion.

Vyn Reese: Okay. Thank you. I'll open the meeting out to discussion.

Jeff Graham: Dr. Reese, I think we can let Marian go. She's on the phone.

Vyn Reese: Oh, Marian, yeah. Thank you, Marian. Sorry. You can go.

Marian McDonagh: Okay.

Patti Varley: This is Patti Varley and I guess I feel a need to make a comment; not necessarily a question, but a… sort of a summary thing and Duane it kind of points to your point that I feel like that is my mission as I sit here right now, which is the safety and efficacy of medications, not necessarily cost at all. Just really that thing. So I wrote a few things that I just feel like this class is really near and dear to my heart, but also I think has some unique issues that are quite concerning to me from a safety and efficacy point of view as well.

First of all I think if no one else in this room was stunned by the preschool age N of 31 kids being looked at… I still am and I'm a pediatric psych person. So for me the first question I think to raise from a safety and efficacy point of view for consumers is the appropriate diagnostic categorization and identification of patients and I think my concern in this class is sometimes the utility of these agents when that particular first thing is not accomplished, which is a clear assessment and diagnosis appropriately of clients of any age being put on these agents. These agents are wonderful, but they are not without an incredible high risk of side effects and in my personal lingo clinically I look at these as cannons as opposed to lasers. They really have a robust consequence on… in side effect profile for patients yet should be available absolutely when necessary. But I think making sure they are utilized appropriately by appropriate diagnosis.

Secondly, the lack of, I agree with the appropriate look at dosage comparisons but also long-term studies, looking at the weight gain of somebody over eight weeks on this agent is not nearly what we see clinically when we see someone on these for a year or two years in dealing with metabolic syndrome.

I think compliance is an absolute issue. You can't really assess an agent unless we know that it has been taken appropriately at the appropriate doses. I feel like side effects – we're constantly being told the new one has less, the new one has less, only to find out later you have the same side effects or worse with new agents than you did with old ones and only time will tell us. So I think when I think about patient safety I think about a track record of known is really helpful in being able to predict the future if I have a good track record.

And I think the other thing I'm concerned about with these agents and the way they're being used in a broader range is the issue of, "If you don't look, you don't see," and people aren't looking for EPS in these patients because there's this misunderstanding that they don't bring the risk that the older agents did. And yet we find that if we start to look more carefully that these symptoms are there and these side effects are there.

I think people have said very clearly, both stakeholders and the presentation, that there isn't any way to predict in these patients who are very acutely ill about which agent is going to work or not, that there isn't one shoe fits all. But I think the idea of not looking at the long-term safety and efficacy of agents that are well known, well understood, been used for a while, which sometimes are the older agents and sometimes, you know, for sake of just argument might be cheaper agents. To just say that those don't play a role I think in this very complex diagnostic category where trying to find something that works for a patient is there is really also a false presentation of newer is better or the more expensive one is better. I think that this is such a diversity and I would just say that the… a comment that was made and I agree, which I think is a separate issue, but I feel like in this category when you have the complexity of these patients and the diversity is that when and if the steps are followed the other system, I think, I will just put a plug in for, is the prior authorization thing being put into place in a way that when it's appropriate, when it's needed it's done in a user friendly way because I think a lot of the steps to get there might be better served if that were an easier service. Thanks for listening.

Vyn Reese: Thank you.

Duane Thurman: This is Duane and I just feel like I have to push back a little bit and say that is the appropriate role for the Drug Utilization Review Committee, but I mean your comments are well taken. But I really need to preserve the distinction between no cost talk here.

Vyn Reese: Hi. This is Dr. Reese. I'm looking back to the last motion. I'm going to focus you on the prior P&T motion. One problem with these agents is they're not all approved for the same indication. Some are approved for bipolar, some are approved for schizophrenia, some have a major depressive disorder inclusion, others don't. So I think when we make our next motion we need to be certain that we place in the motion that they're on the list for the indications for which they are FDA approved.

Also I think we… major depressive disorder wasn't listed in our prior motion. I think we probably need to include that based on this evidence. So anyway those are just a couple of comments I have just looking down

the road to the actual motion. Any other discussion on this very complicated list?

Barak Gaster: This is Barak Gaster and so just following up on that comment I would just point out that on the Preferred Drug List there is no indication by each agent. So I mean the entire class is either on the list or not without indication for… without specification of the indication for each drug.

Vyn Reese: We've done a blanket statement before just saying for the indications for which they are FDA approved. So that's… we've done that before with other drug classes.

Barak Gaster: Okay.

Patti Varley: This is Patti Varley and I know you intended this in your comment, but not just by diagnosis, but by age because there are agents that are FDA approved for child and adolescents.

Carol Cordy: This is Carol Cordy. Just a couple of other house cleaning things on this list. Paliperidone on the top list, on the new list, just indicates the long acting. So I think we need to either put paliperidone like with the ziprasidone as all formulations.

Vyn Reese: I think that was just a new drug that was added to the list. That's all. It was in the prior… the old… the old one is on there.

Carol Cordy: The old one isn't on there.

Vyn Reese: The old one is on there down below.

Carol Cordy: Yeah, but we're dealing with the one on top with the new list. And then one other thing. I'm assuming that the two new drugs, as well as the long-acting paliperidone will automatically go on the Preferred Drug List? This is just if they won't?

Jeff Thompson: This is Jeff Thompson. Only if you suggest that they be on the Preferred Drug List. That is your responsibility.

Carol Cordy: Okay. And then one other thing. It looks like just in the old proposal autism it seems like should be probably… be replaced by pervasive development disorders, which is what…

Patti Varley: If you want to be in the new nomenclature it would be autistic… ASD, autistic spectrum disorder.

Carol Cordy: Okay. Rather than pervasive developmental disorders?

Patti Varley: Yes.

Donna Sullivan: So this is Donna Sullivan. Then we can't go back and change the old motion because that's the motion that you passed the last meeting. So that's just something you'll have to take into consideration with today's motion.

Vyn Reese: That's what we were discussing.

Carol Cordy: That's what I was discussing is just changing the motion and changing the list so that it matches what we're doing.

Patti Varley: That's D not T.

Vyn Reese: Is there any other discussion?

Barak Gaster: This is Barak Gaster. We also have to adjust the populations for the evidence that we reviewed. And so I think the new ones are major depression in adults.

Deb Wiser: This is Deb Wiser. Kind of a general question for the committee. For the treatment of bipolar disorder with the different subtypes should we be differentiating the mixed mania type versus the depressive type since there are different indications for different medications? In other words risperdal is indicated for the mixed type, but not the depressive subtype. It was a comment from a letter that someone had given us. But in re-evaluating that it seems to be the case where it's only indicated for the one subtype of bipolar disorder.

Vyn Reese: This is Dr. Reese. I think if we include at the end for the indications for which they are FDA approved that will cover that comment or that concern so that you can't prescribe a drug that isn't approved for that specific illness.

Barak Gaster: So this is Barak Gaster. I guess I'd be willing to take a stab at a new motion.

Vyn Reese: Okay. Go ahead. This is Dr. Reese.

Barak Gaster: After considering the evidence of safety, efficacy and special populations for the treatment of schizophrenia and bipolar disorder in adults and adolescents; major depression in adults; behavioral and psychological symptoms of dementia; youths with autism spectrum disorder and disruptive behavioral disorder, I move that aripiprazole, asenapine, clozapine, iloperidone, olanzapine, paliperidone long acting injection, quetiapine, risperidone and ziprasidone all formulations should be included in the Washington Preferred Drug List. Atypical antipsychotics cannot be subject to therapeutic interchange in the Washington Preferred Drug List.

Patti Varley: This is Patti Varley. Can we discuss before anybody seconds it because we…

Vyn Reese: Yeah. I think you can amend it or we do friendly amend.

Patti Varley: We didn't include in that lingo the FDA for those… or the lingo you were going to use about FDA approval and I don't see it in there.

Vyn Reese: Right. That should be after preferred… including the Preferred Drug List for indications which they are FDA approved should be after that.

Patti Varley: A semantical error I think when you were speaking of one of them you said the XL formulation but I think you meant all formulations. Is that correct?

Barak Gaster: So under paliperidone I said the long acting and it should be…

Vyn Reese: It should be all.

Barak Gaster: Oh, it should be all. Okay, great. Got it.

Patti Varley: It says all there but I think you said XL formulation. So I just want to clarify. What you said is different than what's up there and what do we want to have there?

Barak Gaster: Right. I was reading from the list of what we…

Patti Varley: Okay. But we agree that we want to change it to all, correct?

Barak Gaster: Great. Good. Yeah, thanks.

Patti Varley: Okay.

Vyn Reese: Any other amendments?

Barak Gaster: This is Barak Gaster. I guess this is just confusing to me. The question of whether the… the wordage about FDA approved indications should be linked to the Preferred Drug List seems fuzzy to me since nowhere in the Preferred Drug List does it have anything about indications. And so I like having those words in there, but I wonder if they should instead be that they are efficacious for their FDA approved indications rather than they should be on the Preferred Drug List for their FDA approved indications?

Chuck Agte: This is Chuck Agte with MPA and I would like to ask that clarification of the board because currently our application of the Preferred Drug List wants it as determined that a client needs an atypical psychotic. We do not look specifically at those indications at this point in time. So depending on how you intend for us to proceed it would depend on whether or not your intent is that there use be limited to their FDA indications.

Barak Gaster: Right. And so I guess those words got missed. So after the list of the different drugs I think we missed the words… there's the list of drugs and then immediately after the list of drugs should be the words "are

efficacious for their approved FDA indications and should be included in the Washington Preferred Drug List."

Susan Rowe: This is Susan Rowe. I agree with that.

Vyn Reese: That sounds like a good amendment.

Jeff Graham: There's a question over there.

Man: I just had a question regarding olanzapine. Do all formulations apply to olanzapine?

Man: I'm sorry.

Man: Does all formulations apply to olanzapine as well since…

Vyn Reese: Yeah, it should.

Man: Okay. It does.

Vyn Reese: You can add that to olanzapine.

Carol Cordy: Maybe the "all formulations" should somehow apply to all of these.

Patti Varley: That's what we were just talking about. I think you're right.

Vyn Reese: More are going to be coming out.

Carol Cordy: Yeah. So just somehow at the end say, "All formulations of all the above."

Patti Varley: Uh huh.

Barak Gaster: This is Barak Gaster. Patti, is it autistic spectrum disorder or autism spectrum disorder?

Patti Varley: Oh God, checking my memory.

Carol Cordy: Do you want to Google it?

Patti Varley: Anybody have a computer?

Carol Cordy: Let's Google it.

Woman: Autism.

Patti Varley: Autism. They just keep changing names of things to keep my brain…

Carol Cordy: And is it capitalized?

Patti Varley: Yes.

Carol Cordy: Disruptive Behavior Disorder is capitalized.

Man: Autism Spectrum Disorder.

Patti Varley: Yes.

Vyn Reese: This is Dr. Reese. Are there any other amendments? Is there a second to Barak's motion as amended?

Carol Cordy: Should we read it again?

Vyn Reese: Barak, do you want to read your motion?

Barak Gaster: After considering the evidence of safety, efficacy and special populations for the treatment of schizophrenia and bipolar disorder in adults and children; major depressive disorder in adults; and children and adolescents with Autism Spectrum Disorder or Disruptive Behavior Disorders, I move that all formulations of aripiprazole, asenapine, clozapine, iloperidone, olanzapine, paliperidone, quetiapine, risperidone and ziprasidone are efficacious for the approved FDA indications and should be included in the Washington Preferred Drug List. Atypical antipsychotics cannot be subject to therapeutic interchange in the Washington Preferred Drug List.

Patti Varley: This is Patti Varley. I'll second.

Vyn Reese: This is Dr. Reese. The motion has been made and seconded. All those in favor…

Jason Iltz: Can we have a discussion really quick? Sorry, I just want to clarify one thing.

Vyn Reese: Sure.

Jason Iltz: This is Jason. For the folks that are administering this policy, the way this motion is written there are some medications currently that are on expedited prior authorization. Does this particular motion modify that in any way or would those remain as part of an EPA process? Is there, you know, appropriate maybe PA processes that may be put on some of these if that's what's deemed appropriate? What does this do from this motion?

Chuck Agte: This motion since it specifically refers to the preferred or non preferred status of the drugs in question would not directly modify a current EPA criteria. At this time we do have expedited authorization criteria that has to be satisfied for the injectables which were already included on the list. So further direction in regard to that I think would be appropriate for the DUR board. In this regard, this motion doesn't impact the way we limit the use or require a PA for appropriate use of the injectables.

Jason Iltz: And then just one more point. Putting… saying they should be part of the Preferred Drug List does not… making a statement that they should be preferred or non preferred on the list. Correct?

Chuck Agte: Correct. I didn't say that entirely accurately.

Patti Varley: Again, our job is to say that when we evaluate the evidence that as far as the evidence says they are all equally safe and efficacious and none of them stand out as being not safe and efficacious as a group. What they do beyond that lies on their policies. Our job is just to say within the group from the evidence we have do they meet that requirement?

Donna Sullivan: This is Donna Sullivan and I might be shot for saying this, but I think in the past this particular motion has been interpreted as you directing to make them all preferred on the list and that is how it has been implemented unless the atypical had not been included in the OHSU review.

Jason Iltz: This is Jason. That's why I asked the question, you know, I think it's subjective when you say, "I move that all formulations…" I think it could be misread or misconstrued. I just think maybe we should go back and make it more clear that we're adding these to a PDL list and we are not making any statements about which one should be preferred or non preferred based on safety and efficacy.

Barak Gaster: This is Barak Gaster and this just gets to the confusion about having a preferred drug list and then some drugs on it which are preferred and others that are not preferred on the Preferred Drug List. Pointing out again the confusion in that terminology. But… and so the way that I read this, and I don't believe it should be open to misinterpretation, notwithstanding that confusing terminology is that all we're saying is that these are drugs that should be on the Preferred Drug List and we're making no statement about whether they should or should not be preferred drugs on the Preferred Drug List.

Duane Thurman: This is Duane Thurman. Actually, the way that we have consistently interpreted this class is that because there is no therapeutic interchange and that there is no, you know, there's no one clear winner or one clear bad drug that what you're statement says is that these all have to be preferred on the Preferred Drug List. The only thing I would change is instead of saying, "in the Preferred Drug List," would be "on the Preferred Drug List." If you want to make it really clear you could say that they are included as preferred on the Washington State Preferred Drug List. I'm sorry for how awkward that is, but that's the way we consistently applied it. On top of that then there was the generics first initiative. On top of that there are various appropriate utilization stops and I think that including… in this motion the FDA requirements I think it actually gives the agencies a more clear objective in implementing any of those utilization requirements.

Jason Iltz: Thank you for that clarification.

Carol Cordy: This is Carol Cordy. I had one more question. Several of the stakeholders pointed out that prior authorization was difficult with these medications. I guess my questions are will this change it and how does the being an endorsing prescriber affect the ability to get…

Duane Thurman: This is, you know, again I think that that's appropriate to talk about in the Drug Utilization Review Committee. This is simply the… this is just the attempt to put what the evidence says about what we want to do with the drugs that we have to make preferred. The questions about whether the Provider One system has issues are separate from this discussion. I would encourage you to, you know, query the department this afternoon. But I think for this point we're getting into the complexities of how to administer and utilize the drugs rather than select them for the purposes. And we have to remember that this also does apply for the other two agencies – L&I and the Uniform Medical Plan and so there are differences in the way that we do this. But this decision affects others and I'll let Donna talk.

Donna Sullivan: So I just want to clarify Dr. Cordy that in the past and Chuck correct me if I'm wrong, the Invega Sustenna was on prior authorization because it had not been officially included in the OHSU review. Today's review does include it so it will now be a part of the class and no longer subject to prior authorization once that coding is in place. The question will be is based on the criteria that we have for putting the injectables on EPA of whether or not it will be an EPA drug. And because I'm so new to Medicaid I can't answer what that criteria is. Chuck, please.

Chuck Agte: Donna is correct in that this… your decision today will have a small impact on prior authorization because not all of these drugs were included as part of the class due to not having been previously studied. And currently the other injectable atypical antipsychotics have expedited authorization criteria specific to their labeled FDA indications and that would be something that we would look at outside of this meeting or with direction from the DUR board as to whether to continue to treat them the same in that manner, or if we make any changes to that existing policy of how the injectables are controlled.

Duane Thurman: And the final question about endorsing practitioners is that because there's no therapeutic interchange allowed here it's not a relevant factor for this drug class. We would not switch. So there's no point… you write for the drug, you get the drug subject to the edits.

Vyn Reese: Okay. This is Dr. Reese again. There's been a few minor changes in the motion. I'm not sure that it needs to be re-read again…

Jason Iltz: I think though that the amendment was based on the discussion it would say, "for their approved FDA indications and should be on the Washington Preferred Drug List."

Barak Gaster: Not included as preferred, but just on the list.

Donna Sullivan: This is Donna Sullivan. Now that introduces some ambiguity. Is your direction… do you want them preferred on the Preferred Drug List?

Barak Gaster: That is what we want to be left up to you and that was per Duane's thought of… rather than saying in, saying on. We don't need every generic formulation, we don't need every brand and generic. I mean…

Jeff Thompson: So I'm going to… all right. Let's talk about the rules under 6088. When you make a preferred status that typically means that it is available to all endorsing providers and the way I interpret that you are saying, "No other criteria." You get it, you write for it. If you make it non preferred or we make it non preferred and you are an endorsing provider and write DAW you can get it without going through prior authorization. If you say they are all preferred we have interpreted that to mean that we don't do prior authorization on these drugs and that includes PA or EPA. And the way I've… EPA is expedited prior authorization, which is a code that can be put into the pharmacy system so it goes through without calling the physician. PA means the physician has to interact with the agency in some way, shape or form to justify the medical necessity. And so I think you need to be clear about whether, you know, you want to give the agency latitude to do prior authorization based on, you know, evidence that is outside of… because you need to say it is preferred or non preferred. You have to say that in the motion or be very instructive of the agency, especially in this class.

Duane Thurman: This is Duane. I think we need to really focus on what's going on here. Okay? Consistently these drugs have all been preferred. Okay? The question is… when you say, "We want you to pick which ones are preferred," what we're asking, "Is there any evidence today that tells us that we can make a distinction between any of these drugs for their FDA indications?" My interpretation of your discussions is that there is not. So we do not have a basis to make any distinction between these on the clinical evidence that's been proposed. Normally we would do a cost analysis. In classes where you say that the evidence says, "We can't tell. They should all be available," then they're all on. Okay? And the, you know, under 6088 as Jeff says the idea is that you will not have prior authorization and the example of that is one of the new drugs was on prior authorization because it hadn't been in the prior report. The purpose of the update was to include that the prior authorization won't be there but there… we still can use safety edits and other utilization review methods to make sure that the drug is being appropriately dispensed. On top of that you're going to talk about generics first other than that.

Vyn Reese: Okay. So it should be… and should be preferred on the Washington Preferred Drug List?

Duane Thurman: That would be our understanding.

Vyn Reese: So let's put that back in. We need to move along. We are way over time. We're not going to have time for the rest of our agenda if we don't move along here. So should be preferred on the Washington Preferred Drug List. Do you want to do preferred drugs or preferred?

Man: Preferred.

Vyn Reese: Preferred is fine. Okay. Any other amendments?

Jason Iltz: I know we're behind, Vyn, but this is Jason again. I just have to ask the question, currently right now the list has preferred and non-preferred medications…

Duane Thurman: Not in this class.

Jason Iltz: Yes it does. Where it comes in is from the status of a generic versus a brand. And so does this change that? That's my whole point is I don't think our intent when we say "all formulations" we don't mean generics and brands. So does the generics first policy help us here with that?

Donna Sullivan: I'm not going to speak to the generics first policy but for the Uniform Medical Plan and the Aetna Public Employees Plan our benefit design makes any multi-source drug a non-preferred drug. It's in tier three at the highest cost tier and generics are in tier one. So I don't feel that this motion requires us to cover any multi-source products that are out there where there isn't a generic equivalent available. Jeff?

Jeff Thompson: I believe under generic substitution the pharmacist would substitute the generic for the brand where it was AB rated under our DOH substitution law and if there was a DAW in that request then there would… there would be a decision made at the pharmacy and perhaps with the agency, which has been the case with all drug classes when it gets to this issue.

Duane Thurman: I guess to make it more complicated that's why we originally had all formulations for specific drugs to eliminate that problem. We can reinsert that because the intent is not to require a brand where there's a generic as preferred. You're absolutely correct.

Jason Iltz: And so just to clarify so if there is a… both a brand and a generic available those are not different formulations, those are different sources of the same formulation?

Jeff Thompson: And just for the clarity of the audience here, I will bring to you at the discussion of generics first what our EPA criteria are based on FDA indications and ask you to opine on whether you want to continue those so that we are ensuring the safety of our clients that they are getting these injectable drugs for the FDA indications and if you want to then open it up for off label indications you can instruct us and we'll have a discussion about that during the DUR portion.

Duane Thurman: We're going to put the all formulations back in. Why don't you go ahead with your break and you can make the final…

Vyn Reese: I think we should get this done before our break. We only have a short break now anyway because we don't have time for the regular break. So all formulations are in there I think aren't they?

Barak Gaster: Well all formulations is already at the top. I move that all…

Duane Thurman: No. We want it by specific drug.

Carol Cordy: So the question is are there other formulations of some of those others?

Donna Sullivan: We could go back and make sure that they are appropriately applied.

Patti Varley: This is Patti Varley. I'm confused why we can't say the way it was before, which is just have it all formulations and then the list?

Duane Thurman: We want to make it clear that we do not have to have the brand form of risperdal as preferred.

Vyn Reese: It doesn't say that though.

Duane Thurman: I just want it extremely clear.

Christine Klingel: This is Christine Klingel. Is there a way… I mean we're saying formulations versus IM versus PO. Correct? So could we distinct that formulation versus a brand generic formulations? So the dosage form instead of brand generic?

Donna Sullivan: We could either do potentially all dosage forms or routes of administration.

Vyn Reese: Why don't we just do all routes of administration? That way we can take out all formulations. Then we can leave off all formulations. Okay. Now any other discussion or amendments? Okay. This motion has been made by Dr. Gaster and seconded by Varley, ARNP. All those in favor of the motion say, "Aye."

Group: Aye.

Vyn Reese: Opposed, same sign. Motion is passed. We'll take a five-minute break and be back in five minutes.

Okay, the next item on the agenda is the drug class review on the newer antihistamines. Do we have somebody on the line for this now or it's a… isn't it a…

Donna Sullivan: This is Donna. I think it's a recording. Regina is right behind you to help you.

Regina Chacon: This is a recorded presentation and we will put it on as soon as you are ready.

Vyn Reese: Okay. Everyone have a… get a chance to take their seats. This is Dr. Reese. We're going to reconvene and we're going to go through the drug class review on the newer antihistamines and it's recorded due to OHSU… a simultaneous OHSU meeting. Can we get that dialed up?

Regina Chacon: Are you ready to go?

Vyn Reese: Yeah.

Woman: So this is the second update of our newer antihistamines report. It was completed in March 2010. So I understand that your committee has considered this class before. So I'm going to focus on the information that's new to the update and then any changes to the conclusions based on the new evidence. And in the slides the new information is indicated with underlining.

So if you go to slide 2 shows the included populations and we didn't make any changes to the included populations of this update. We included both adults and children with seasonal or perennial allergic rhinitis or urticaria. Next slide.

This shows our included interventions. We added three new drugs this update. There is a new oral antihistamine approved, levocetirizine. The brand name of that is Xyzel. And then we also added two new nasal sprays – azelastine and olopatadine. Next slide.

This shows our included outcomes and again no changes this update. We focused on patient relevant outcomes such as symptoms and quality of life. And for assessment of safety as usual we looked at withdrawals and specific adverse events. Next slide.

Slide 5. For this update our searches were conducted through November 2009 and after review of abstracts and full text articles we ultimately added 61 new publications. So this was quite a large update report. Next slide.

We can now move on to the results. For our first key question, which addressed comparative effectiveness and efficacy of the antihistamines. Next slide.

Slide 7. So the most direct evidence is available in adults with seasonal allergic rhinitis with a total of 11 short-term head-to-head trials. Five of these head-to-head trials are new for this update and the comparisons that they made are shown on this slide. So we had… for this update new evidence available for the comparisons of fexofenadine versus desloratadine, levocetirizine versus loratadine, and azelastine nasal spray versus cetirizine. For the nasal spray versus cetirizine we previously had one head-to-head trial and now we have a second. And then desloratadine… azelastine nasal spray versus desloratadine and olopatadine nasal spray are the other new head-to-head trials. All of the head-to-head trials were short-term. All but one was two weeks duration. One was four weeks duration and almost all were fair quality according to our internal validity ratings. Next slide.

Slide 8. So the head-to-head trials in adults with seasonal allergic rhinitis found that the antihistamines were similar in efficacy to relieve symptoms with only a few exceptions. One exception was that azelastine nasal spray led to greater symptom relief than oral cetirizine in one trial. But in a second trial that was new this update the difference between the

drugs was not statistically significant. It was 24% improvement in symptoms versus 20% with a P value of 0.08. And then previously we found that patient related symptoms, but not investigator related symptoms were improved more with loratadine than fexofenadine. And really other than that the direct evidence from the head-to-head trials found similar efficacy in their comparisons—similar efficacy among the antihistamines.

Moving on to slide 9 – three of the head-to-head measured quality of life in addition to symptoms; an outcome that might be more relevant to patients than a symptom checklist. In these studies quality of life was measured using a scale that was developed specifically for these trials – the Rhinoconjunctivitis Quality of Life Questionnaire and quality of life was measured at two weeks. So all of these trials measuring quality of life were new for this update. In two studies quality of life scores were better with azelastine nasal spray than with oral cetirizine. And the third study found better quality of life with fexofenadine than loratadine. Next slide.

Slide 10. So in addition to the head-to-head trials, 15 placebo-controlled trials demonstrated short-term efficacy of desloratadine, levocetirizine, and azelastine and olopatadine nasal sprays. I won't go into detail on these trials because they don't add comparative evidence beyond what we have from the head-to-head trials. But they did show efficacy versus placebo. Next slide.

Slide 11. Now we can move on to our next population, which is adults with perennial allergic rhinitis. So less evidence for this population. We identified two head-to-head trials and both of the trials and both of the trials were new for this update. One compared levocetirizine 5 mg to loratadine 10 mg. This is an unpublished trial with results that were available at clinicaltrials.gov and the trial found no difference between the treatment groups on the total symptom score measured at two weeks. So no difference between the two. And then the second head-to-head trial in this population found also no difference between levocetirizine and desloratadine in symptom improvement. Both of them showed efficacy versus placebo in that same trial. They had a placebo

arm as well, but no difference between the drugs. So that's the only head-to-head evidence in this population.

So moving on to slide 12. In addition to the head-to-head evidence we identified one placebo-controlled trial… oh, not one, 10. We identified 10 placebo-controlled trials showing the general efficacy of azelastine nasal spray, oral cetirizine, desloratadine, levocetirizine and loratadine. So not comparative evidence, but general efficacy versus placebo for all of those drugs. And then new this update were two trials that showed improved quality of life after six months with levocetirizine 5 mg compared with placebo. Unfortunately though we have no comparative longer term evidence about quality of life in this population. But two trials found better quality of life versus placebo with levocetirizine. Next slide.

Slide 13. Our next population is adults with urticaria. In this population there are five head-to-head trials including two that were new for this update. Previously we found one trial in which loratadine reduced total symptom score more than cetirizine but found no difference between the groups in response rate. So however a second trial that's new this update found a greater response rate with loratadine than cetirizine in contrast to the previous trial. So also new this update are two trials of levocetirizine. One compared levocetirizine to desloratadine and one compared levocetirizine to cetirizine. In the first trial levocetirizine reduced symptoms more than desloratadine. And although quality of life was measured in this trial they didn't do a head-to-head analysis of the two drugs. So we can't say anything about that outcome. And then in the second new trial its response to a wheal and flare test was better with cetirizine than levocetirizine. Next slide.

Slide 14. Now we can move on to the evidence in children. The first children with seasonal allergic rhinitis. There's really a lack of good comparative evidence in this population. We don't have any head-to-head trials. Placebo-controlled trials that are new this update demonstrated the general efficacy of cetirizine and fexofenadine. Previously we had active controlled trials comparing cetirizine and loratadine to first generation antihistamines and they were similar in efficacy and then loratadine was less effective than fluticasone nasal

spray for nasal symptoms. But that's not new information this update. Next slide.

Slide 15. In children with perennial allergic rhinitis there are two head-to-head trials, one of which is new. One compared cetirizine to loratadine in children ages 2 to 6 years old and the other compared cetirizine to levocetirizine in children ages 6 to 12 years. And the trial in the older children is new this update. So in this new update there was more improvement in total symptom score with cetirizine than levocetirizine, but no difference between the groups in quality of life scores. Previously what we found in the trial in younger children also had mixed results. With loratadine showing better efficacy for parents and investigator rated symptom relief, but no difference between groups in the global evaluation score. So depending on what was measured in this trials either one of the drugs was found more effective or no difference. Next slide.

Children with urticaria – there's no new evidence this update and we still have no direct evidence. Previously we had just two trials and I won't say much about that because there is nothing new. Next slide.

Slide 17. This is key question 2 and in this key question we addressed comparative harms of the different antihistamines. Next slide.

Slide 18. First adults. So the new evidence this update is consistent with our previous conclusions showing low rates of withdrawals for all of the antihistamines. We were able to add the new drugs, but in general the total withdrawals due to adverse event rate was about 2 to 5% across trials. And serious adverse events were rare. New evidence found more sedation with cetirizine and levocetirizine than with loratadine, desloratadine and possibly fexofenadine, but the evidence was mixed for fexofenadine. Next slide.

Slide 19. In adults bitter taste was… and this is new evidence. Bitter taste was more frequent with azelastine nasal spray than with olopatadine nasal spray in one head-to-head trial. Also new, there were no clinically relevant EKG changes found with fexofenadine and desloratadine or levocetirizine. And also new this update there was a

patient who had a… one patient had a nasal ulcer who was using azelastine nasal spray. Next slide.

Slide 20. In children the total withdrawal rates due to adverse events was also low as within adults. It was about 3.1% with the newer antihistamines compared with almost 5% with placebo. There was more sedation with cetirizine and desloratadine than with placebo. And then more cough than with children using azelastine nasal spray than placebo. And then the new data are consistent with our previous findings that there were no cases of clinically significant QTC prolongation with cetirizine, fexofenadine or desloratadine. Next slide.

We're on slide 21. This is our key question 3, which addressed differences among the drugs in subgroups of patients based on demographics and other factors.

So slide 22. We found no new data for this key question on demographics, socioeconomic status or drug interactions. In patients with asthma, asthma did not worsen with cetirizine, levocetirizine, desloratadine or azelastine nasal spray. And in patients with atopic dermatitis there was no worsening of atopic dermatitis and no difference in children with… children achieving developmental milestones when they use levocetirizine compared with placebo. And in pregnant women new data were consistent with the previous findings. There's a low risk of adverse events, adverse outcomes with cetirizine, fexofenadine, and loratadine. And new evidence found that the antihistamines did not significantly increase the risk of hypospadias in infants.

Okay. The next few slides summarize our findings for this update. So I'll just go through those quickly. We're on slide 23. So the summary for adults – first seasonal allergic rhinitis. There's fair quality evidence of similar efficacy for cetirizine compared with fexofenadine and loratadine, for fexofenadine compared with loratadine and desloratadine, for levocetirizine compared with loratadine and for azelastine nasal spray compared with desloratadine and olopatadine nasal spray. There's also fair quality evidence of better efficacy with azelastine nasal spray compared with oral cetirizine for symptoms and quality of life. And then

quality of life was better with fexofenadine than loratadine in one fair quality study. Next slide.

Slide 24. In adults with perennial allergic rhinitis there's fair quality evidence that levocetirizine is similar in efficacy to loratadine and desloratadine. For other comparisons we have insufficient evidence and then we have two six-month trials showing improved quality of life with levocetirizine compared with placebo. And other than the compare- for urticaria in adults other than the comparison of loratadine showing better efficacy than cetirizine we have insufficient evidence to make comparisons among the other drugs. Next slide.

Slide 25. The summary in children there's no comparative evidence in children with seasonal allergic rhinitis. In children with perennial allergic rhinitis there's fair evidence that cetirizine has better efficacy than loratadine and then cetirizine is better… was found better than levocetirizine for symptom relief, but not quality of life and that was in one fair quality study. And no comparative evidence in children with urticaria. And the next slide, slide 26.

Harms in adults – again not too much new information. Discontinuation rates were low among all of the antihistamines. The other new information was there is more bitter taste nasal discomfort with azelastine nasal spray than olopatadine nasal spray in that one head-to-head trial. Next slide.

Slide 27. Harms in children – there's insufficient evidence to make conclusions about comparative harms, but few withdrawals due to adverse events as with the studies in adults. And there's fair quality evidence for safety for cetirizine and loratadine and limited but some evidence on the safety of desloratadine and fexofenadine in children.

And then finally the summary in subgroups – the conclusions did not change this update based on new evidence and we really have insufficient evidence to make conclusions about comparative effectiveness in subgroups and there's fair evidence that there's no comparative difference in efficacy or safety in patients with asthma or

atopic dermatitis. So that's the new evidence and I would be happy to address any questions that you might have.

Vyn Reese: But she can't.

[laughter]

Vyn Reese: I don't have any stakeholders listed who would like to speak. So we'll move on to the motion and discussion.

Donna Sullivan: This is Donna Sullivan. I just want to point out that in the past this drug class has not included the mast cell stabilizers, the inhaled antihistamine formulation. So we would like direction on whether or not you would like to include those within this drug class or not. Because they were included in the review, in the past you have said certain drug cl- drugs do not belong in a class and you can remove them if you wish to or you can leave them in here.

Vyn Reese: This is Dr. Reese. I think they're antihistamines. They're not, you know, mast cell stabilizers. I think azelastine is an antihistamine and olopatadine I think is too so they should be in this drug class because they're not… that was another drug that was a different mast cell stabilizer. These are antihistamines which are different.

Carol Cordy: They're not, of course, wouldn't think used for urticaria.

Vyn Reese: No.

Carol Cordy: But maybe that doesn't matter.

Vyn Reese: They are used for the indications for which they are approved. We went through that on the last one.

Barak Gaster: Yeah. To me… Barak Gaster. The functional question is, "This is a class in which we have definitely wanted there to be therapeutic interchange," and so our… and so we've included the sentence that therapeutic interchange is allowed for this class. And so our question is, "How do we

feel about therapeutic interchange going from a nasal spray to an oral formulation?"

Carol Cordy: This is Carol Cordy again. How difficult would it be to have a separate class… to make a separate class for those two inhalers, two nasal sprays?

Donna Sullivan: This is Donna Sullivan. So to make them a separate class meaning you would make a separate motion for those two products or to… a separate class meaning you just don't include them in this class at all? If you make the motion for them to be a separate class you could make the two nasal sprays interchangeable and then we would be… need to pick one as preferred or not preferred. If you left them in the class then the question is, "Do you want a nasal spray product to be preferred within the class?" I think you could keep them in the same class and just direct us one way or the other.

Vyn Reese: This is Dr. Reese. They've been compared head-to-head. I mean it would just be like another formulation like antipsychotics versus IM versus PO. I mean it's the same class of drug administered in a different way with different indications. I don't see why we would… should take them out of this class. This seems like where they belong.

Barak Gaster: Right. I don't either. I don't either, but I'm just pointing out the fact that if we do keep therapeutic interchange for this class that… and we keep the nasal spray in the class that we are then directing that we feel comfortable with therapeutic interchange going from a nasal spray to an oral pill, which I personally do feel comfortable with. But I'm just pointing out that that is a new functional feature of our motion.

Donna Sullivan: So this is Donna Sullivan again. Going back to, I guess, our issues with the budget. Not to say that this is a cost thing, but if you did include them in the class then they would have to be preferred at this point in time unless you told us to make them not preferred because we are not able to do the cost analysis to determine which one we would select as a preferred agent.

Vyn Reese: So… go by that one more time. So we can… if we approve them and say they can be therapeutically interchanged then we'd have to say that they're what? That they're non-preferred?

Donna Sullivan: Yes.

Vyn Reese: Okay.

Duane Thurman: Again, this is Duane Thurman. I think that the simplest way to look at this is that you continue to say, you know, "Are these drugs comparable? Are there differences?" if you want restrictions on the ability to substitute between different methods of delivery you should make that clear in the motion. Other than that we will worry about what ends ups preferred.

Vyn Reese: Exactly. I mean that's something we haven't done before.

Chuck Agte: This is Chuck Agte. There is precedent because within, for example, the estrogen class we have multiple forms of delivery that you have made motions that they be interchangeable within their mode of delivery. So for example transdermal estrogens you've ruled on that specifically versus oral estrogens.

Susan Rowe: This is Susan Rowe and I think I would be more comfortable with there being therapeutic substitution within the spray class or within the oral class, but not necessarily going from nasal spray to oral.

Woman: I think we agree.

Vyn Reese: Okay.

Thad Mick: This is Thad Mick. One other consideration within this therapeutic category is the fact that many of these agents are available over-the-counter and as to whether or not you want your decision to apply to those agents as well.

Vyn Reese: That was true last time that we looked at the agents. And so I don't… I mean we can give patients over-the-counter medications. Isn't that correct?

Donna Sullivan: Yes. Medicaid currently covers the over-the-counter products. So that's why we continue to include them in the class. I think what we would look at is if you feel a nasal spray needs to be preferred on the list that you call out and tell us that. If not, then I think you need to instruct as well.

Carol Cordy: This is Carol Cordy. I was thinking of sort of a practical thing. If I prescribe a nasal spray to somebody who can't swallow pills or something, if we leave it as they can be interchanged then they could go to the pharmacy and be given a pill.

Donna Sullivan: That is correct.

Carol Cordy: Which isn't necessarily good.

Donna Sullivan: Unless you specifically state that they are interchanged within their route of administration.

Jeff Graham: Yeah. This is Jeff Graham. There is syrup available in all these classes—the oral classes. So I think if somebody can't swallow a pill they could take syrup. And I don't recall if the evidence showed that the nasal sprays are any more effective than the oral ones. So I'm not sure we want to separate them out to give them a preferred status. Is it any matter? That's my opinion.

Barak Gaster: This is Barak Gaster. That is my opinion as well and in the very rare clinical situation in which someone needs a spray because they can't swallow a pill then that therapeutic interchange could be overruled in that very rare situation. And so I personally would feel comfortable having these all be in the same class and subject to therapeutic interchange from a nasal spray to an oral pill. You know, that notwithstanding the odd window that we're in, in which you're saying that there would not be an availability for that therapeutic interchange because they would be automatically preferred on the preferred class. I can't speak to that difficulty.

Chuck Agte: This is Chuck Agte again and in your considerations, and if I'm wrong hopefully one of the pharmacists on the board can tell me, but I believe

that there would be difficulty for a pharmacist receiving a… if at some point some were chosen as preferred and some were chosen as not preferred, for a pharmacist to take a prescription for a nasal spray and determine the appropriate interchange to an oral medication. I'm not sure how that would work for you. So I guess I'm posing that as a question for you guys to consider in your deliberation.

Christine Klingel: This is Christine Klingel, pharmacist. Yeah, I'm trying to think. I know you brought up the estrogens as one example, but I can't think of another class beyond that where we are expected, as pharmacists, to make that decision. I mean fortunately most of these do have standard adult and standard pediatric doses. So I think it would be, you know, easier probably than an estrogen which is a difficult think to interchange versus a, you know, you could say a standard adult dose of a nasal spray, a standard adult dose of a tablet versus pediatric doses. I think the concern would be, you know, if you had a pediatric child you would obviously not be wanting to switch an infant to a nasal spray or something like that, but I would think beyond that I would think Washington pharmacists could be capable of doing that.

Jason Iltz: This is Jason. I would agree with Christine.

Vyn Reese: After all these… this discussion does anyone… this is Dr. Reese. Does anyone want to craft a new motion?

Ken Wiscomb: This is Ken Wiscomb. I don't mean to throw a wrench into this, but if we're sort of looking at this class, if we're going to expand the antihistamine class to look at drugs that effectively treat allergic rhinitis, would we not include Singular tabs as well, which is also…

Vyn Reese: That's a different class of drug. That's not an antihistamine.

Donna Sullivan: It's a leukotriene.

Ken Wiscomb: It's a leukotriene inhibitor, but… it's not an antihistamine but we are including mast cell inhibitors as well.

Woman: Which is an antihistamine.

Ken Wiscomb: Huh?

Woman: That's an antihistamine.

Vyn Reese: All these drugs are antihistamines on this list. The leukotriene inhibitors aren't on the list. There are none on this list.

Vyn Reese: Okay. I'll go ahead and try to do this. Okay? I'm going to be open to amendment given the complexities of the interchanges.

After considering the updated evidence of safety and efficacy in special populations and newer antihistamines for the treatment of seasonal allergic rhinitis, perennial allergic rhinitis and chronic idiopathic urticaria, I move that cetirizine, desloratadine, loratadine, fexofenadine, levocetirizine, azelastine nasal spray, and olopatadine nasal spray are safe and efficacious. The Washington Preferred Drug List should contain a product that is non-sedating and an FDA approved product for pregnancy category B, and must make available a FDA approved product for the special population of patients 6 months to 2 months of age.

Barak Gaster: Two years.

Vyn Reese: Two years. I'm sorry. Newer antihistamines can be subject to therapeutic interchange. Now this is where I should put in both an oral and an intranasal category. Or how do we want to phrase that? That's the question.

Donna Sullivan: If you feel a nasal spray needs to be preferred on the list then I think you need to tell us that one of them needs to be preferred and we will make that…

Vyn Reese: But we don't feel that they need to be preferred.

Donna Sullivan: Then I think you can just leave it the way it's written and we will…

Vyn Reese: Okay. Then you can do it. And I think that's perfectly adequate.

Barak Gaster: I agree.

Deb Wiser: This is Deb Wiser. I think we do need to make an exception for chronic urticaria and the nasal sprays though.

Vyn Reese: We could just say…

Woman: They are labeled indications.

Vyn Reese: What if we did that before?

Man: [inaudible]

Vyn Reese: Yeah. Are safe and efficacious for the… for their FDA approved indications. That should be on the top. So we'll go ahead… we will not separate them out. We'll go ahead and say, "Newer antihistamines can be subject to therapeutic interchange in the Washington Preferred Drug List for the treatment of seasonal allergic rhinitis, perennial allergic rhinitis and chronic idiopathic urticaria." Any amendments?

Deb Wiser: This is Deb Wiser. I second.

Vyn Reese: The motion has been made and seconded. All those in favor say, "Aye."

Group: Aye.

Vyn Reese: Opposed, same sign. Okay, the motion is passed.

Donna Sullivan: This is Donna Sullivan. We won't be doing a cost analysis so there will be no… there will be no means for us to make them preferred because we will not be doing a cost analysis. So they will not be… there will be no change to the PDL other than these will now be included as a part of this class.

Vyn Reese: Okay. So now we're going to be launching into the scan portion of the agenda and it's been pointed out to me that one of the speakers this afternoon is ill and so we can move some of the agenda to the afternoon. So what we'll do is we'll go through as many scans as we can until 12:30

and then we'll adjourn and do our DUR board work after lunch and then re-convene as the P&T Committee later to finish the rest of the scans. And so the next item on the agenda is the oral hypoglycemics. I'm going to be reading this scan. So this is the drug class review on oral hypoglycemics. Next slide, please.

History – date of last update was update 2 completed in May 2005. Dates of previous preliminary updates were scans for update number 3 in May 2009, February 2008 and January 2007. Next slide.

Inclusion criteria – population: adults with Type 2 diabetes. Interventions: sulfonylureas, which are chlorpropamide, glimepiride, glipizide, Glyburide, tolazamide, tolbutamide (both immediate and extended release formulations included); short-acting secretagogues: repaglinide and nateglinide. Next slide, please.

Inclusion criteria – effectiveness outcomes: lowering of hemoglobin A1C, clinical relevant outcomes, time to requiring insulin, progression or occurrence of long-term microvascular or macrovascular diseases, exercise tolerance, complications of diabetes, all-cause mortality, and quality of life. Harms were overall adverse events, withdrawals due to adverse events, serious adverse events and specific adverse events. Next slide.

FDA and Health Canada website searches – there were no new drugs, no new indications and no new black box warnings. Next slide.

Literature search – controlled clinical trials: Medline January 2009 to August 2010. Comparative effectiveness reviews in AHRQ and CADTH websites. Next slide.

New literature – controlled clinical trials: Overall new citations is 59; new potentially relevant trials are 4; new publications from previous scans were 13. Comparative effectiveness reviews: update in progress of July 2007 AHRQ Effective Healthcare Program review on oral diabetes medication with Type 2 adults… or adults with Type 2 diabetes. That's it.

So I'll take a motion to approve the scan. Oh there's… let's have a motion to approve the scan.

Christine Klingel: This is Christine Klingel. I move to approve the scan.

Vyn Reese: A second?

Barak Gaster: Don't we have one stakeholder?

Vyn Reese: We're just approving the scan right now.

Barak Gaster: Oh, all right.

Jason Iltz: This is Jason. I'll second.

Vyn Reese: All those in favor say, "Aye."

Group: Aye.

Vyn Reese: Scan's approved. We do have one stakeholder, Long Nguyen of GlaxoSmithKline.

Long Nguyen: Good morning. My name is Long Nguyen, PharmD representing GlaxoSmithKline on behalf of Avandia. My presence here is to address… to bring to the committee the latest announcement by the FDA that you may or may have heard already…

Vyn Reese: Avandia is not in this class.

Jeff Graham: And we will be discussing this issue after lunch.

Long Nguyen: Okay. Okay.

Vyn Reese: Thank you.

Long Nguyen: Thank you very much for the clarification.

Vyn Reese: Any other discussion? I'd like to turn your attention to the prior motion, which is in your pamphlet—your brochure. Doesn't look like to me there's been any new data so if somebody just wants to re-state that and make the motion that's fine.

Barak Gaster: This is Barak Gaster. I move that we reiterate the prior motion dated October 21, 2009.

Vyn Reese: Is there a second to that?

Carol Cordy: This is Carol Cordy. I second.

Vyn Reese: All those in favor say, "Aye."

Group: Aye.

Vyn Reese: Opposed, same sign. That's approved. The next scan is on the skeletal muscle relaxants. Okay. This is the drug class review on skeletal muscle relaxants. Update 3, preliminary scan 4. Next slide.

History – original report was in September 2003. Update number 1, January 2004; update number 2, May 2005 with searches through November 2004. Previous update scans were update 3, scan 1 February 2007; update 3, scan 2 March 2008; and update 3, scan 3 June 2009. Next slide.

Inclusion criteria – populations: adults or children with spasticity or a musculoskeletal condition. Excluded was restless leg syndrome and obstetric patients and those on dialysis. Next slide.

Inclusion criteria – interventions were baclofen, carisoprodol, chlorzoxaxone, cyclobenzaprine, dantrolene, metaxalone, methocarbamol, orhpenadrine and tizanidine. Next slide.

Inclusion criteria – effectiveness outcomes: relief of muscle spasms or pain, functional status, quality of life. Excluded were non-clinical outcomes such as electromyogram or spring tension measurements.

Harms were adverse events, withdrawals and specific adverse events. Next slide.

FDA and Health Canada website searches – no new drugs, no new indications and no new safety alerts. Next slide.

Medline search – date range from May 2009 to August 31, 2010. Total new citations found in this scan were 15. Next slide.

Selection study – potentially relevant new trials were 2. There were two placebo-controlled trials described in one publication of cyclobenzaprine extended release in patients with muscle spasm associated with low back and neck pain. Carisoprodol 250 mg versus placebo in another trial and carisoprodol 350 mg in patients with low back pain. That was a comparative study. Previous scans did not identify any potentially relevant trials. Next slide. So that's it. And I have no stakeholders, I believe, on skeletal muscle relaxants.

Barak Gaster: I move to approve the scans. This is Barak Gaster.

Vyn Reese: And a second?

Woman: I'll second.

Vyn Reese: All those in favor say, "Aye."

Group: Aye.

Vyn Reese: Opposed, same sign. Okay. The next item on the agenda…

Barak Gaster: Wait. Motion?

Vyn Reese: Oh. Sorry, I'm even going faster than we have to go. Let's discuss this. Look at the prior motion.

Barak Gaster: It's a little bit fuzzy. I think we need to re-create this one.

Vyn Reese: What happened to this one?

Barak Gaster: Garbled.

Vyn Reese: It looks like a… it's only a partial motion. Do you have any comment on this motion?

Barak Gaster: It's kind of weird that Soma is on here at all.

Susan Rowe: It's covered in the first sentence. This is Susan Rowe. It's taken out in the first sentence.

Barak Gaster: Right. Yeah, yeah, sure, but it's funny that we're even…

Vyn Reese: This is Dr. Reese. It's not been taken off the market yet and so… and actually there was a new trial regarding it too. But it's certainly one we ask not to be on the list in the prior meeting.

Woman: And it's not on the Preferred Drug List, right?

Vyn Reese: No.

Susan Rowe: This is Susan Rowe. I think a recent development also is that it has become a scheduled drug.

Barak Gaster: The concern is abuse with this medication. It's metabolized meprobamate and so from a safety standpoint the committee, the very first time this was reviewed, and this motion goes back to a committee member that was the very first part of the… this process, and that was the concern that it would not be part of the Preferred Drug List, it would be excluded from the list and a non-covered drug. So I think it's still appropriate that we keep that in there. I do think we should craft the motion so that it fits the outline that we typically use, but again all of the things that are up there, in my mind, are still considered to be appropriate and they were specific to spasticity for a couple of the medications when we originally reviewed them and then the other ones were specific to just muscle relaxation. So that's kind of why we broke them out the way we did. Or tizanidine and baclofen or, you know, for other particular indications of, you know, MS and things of that nature

where the other ones are more for chronic pain type syndromes that have to do with muscle.

Vyn Reese: Right. And that's why it was broken up this way before. This is Dr. Reese. So do you want to… do you want to go ahead and tackle that since you brought that up? Do you want to make… do you want to…

Barak Gaster: I'm trying to find our motion template here.

Carol Cordy: Yeah, let's use the motion template.

Vyn Reese: Yeah. We have to re-phrase this.

Barak Gaster: So this is Barak Gaster. So after considering the evidence of safety, efficacy and special populations for the treatment of spasticity, I move that tizanidine and baclofen are found to be efficacious and safe and for the indication of muscular skeletal relaxation methocarbamol, cyclobenzaprine, metaxalone and orphenadrine are found to be safe and efficacious. The committee finds that carisoprodol is subject to abuse and should not be covered. I therefore move that tizanidine, baclofen, methocarbamol, cyclobenzaprine, metaxalone and orphenadrine should be included in the Washington Preferred Drug List.

And then I guess we should discuss as a committee what we think about therapeutic interchange for these.

Jason Iltz: Does saying, "Not covered" is that clear or should we say something to the effect of, "And should not be part of the Washington Preferred Drug List?"

Chuck Agte: This is Chuck Agte with MPA. I believe that you would have a couple of options. You could either say that it is not to be part of the list or you could specifically say it is to be part of the Preferred Drug List and never preferred.

Donna Sullivan: So this is Donna. The original reason why you said it not to be covered was so that Medicaid would actually be able to not cover it. So we do need that language in there to allow Medicaid to not cover it unless you

decide that it's not included in this class. If it's not included as part of this class then each agency is able to treat the drug based on their own business decisions.

Chuck Agte: And this is Chuck Agte. Actually, the covered language is a little bit problematic. That's why I suggested you add the route of either excluding it from the class or saying it's part of the class and not to be preferred because Medicaid technically, regardless what you direct, it is a product with a signed federal rebate agreement and we must consider it for coverage. So we can be very, very tight about our criteria on it, which we are currently, but we don't actually have the option to say, "We will never pay for it."

Vyn Reese: This is Dr. Reese. The way it is phrased now it sounds like it is in the class, but should not… that we recommend it not be covered or… it not be on the Preferred Drug List because it's subject to abuse and shouldn't be on the Washington Preferred Drug List. So it's the safety issue. It's in the class but not covered because of the safety issue. So it's pretty clear. We've done this with other classes.

Jaymie Mai: This is Jaymie with Labor and Industry. This class does affect us and I think the language right now is clear for us in terms of implementing it. So we definitely have clear directions as to what to do with this drug right now.

Donna Sullivan: When it says not covered is that… so if the preferred… if it's not included in the class, Jaymie, at all what would you be able… would you have clear direction as well?

Jaymie Mai: Not so much. Then it becomes us trying to develop criteria for possible coverage and I don't think that's where you guys are heading.

Vyn Reese: No, no.

Jason Iltz: This is Jason. I think our original intent though was that it would never be covered across all of the agencies. And so it sounds like maybe that… we are not meeting that particular criteria. So what can we do if that's our intent to make it work for everybody?

Chuck Agte: This is Chuck Agte. I believe your language is correct because for those agencies who are not Medicaid that is very clear direction. Medicaid just has to caveat that based on what we are allowed to do. We can't quite make it not covered, but your intent is very clear in that. I believe currently based on the language before out of our, you know, million clients we have four on carisoprodol and it's because we do have to allow some window of opportunity for that product because it is FDA approved and has a federal rebate agreement. But I believe the language of covered… not covered suffices because we will continue to enforce that to the best of our ability within the guidelines that we have to work within.

Barak Gaster: Okay.

Vyn Reese: What happened to our motion?

Donna Sullivan: I'm just copying and pasting this second part.

Vyn Reese: There's some language problems. Yeah.

Patti Varley: This is Patti Varley. If you read the first sentence… yeah, the first sentence, found to be efficacious and safe. Is that what we want it to say?

Vyn Reese: Right.

Donna Sullivan: Or we could just do are efficacious.

Vyn Reese: Right. That's easier.

Patti Varley: That's fine. It just didn't read right.

Barak Gaster: And then… this is Barak Gaster. How do we feel about therapeutic interchange within this class?

Vyn Reese: Is that the way it is now? How is it set up now?

Donna Sullivan: This is Donna Sullivan. Right now we have them broken out. So first spasticity the tizanidine, baclofen can be interchanged for each other. Or for the other indications those can be interchanged. So you do allow interchange but we have broken them out specifically into their different indications.

Patti Varley: So you could say within indication, can be subject to therapeutic interchange within indication?

Barak Gaster: But there's no indication on the prescription and so I think what we need is we need a sub within… a sub within the sub classes by indication. They can be interchanged.

Jason Iltz: That's kinda what we did though, right? Because you said for the treatment of spasticity for both of those and then the indication of… maybe that's not enough.

Barak Gaster: Yeah. Right. And so… actually, the way that she's writing it now is right. So skeletal muscle… or this whole class is called skeletal muscle relaxants. So right. I mean it's almost like the spasticity drugs are almost separate from the class that we are really reviewing, which is muscular skeletal relaxants. And so in the scan do they break those out?

Vyn Reese: The scan did break them out for the indication of spasticity and also the indication of… they just said safe and efficacious. It didn't say whether they could be interchanged.

Christine Klingel: This is Christine Klingel. I noticed in the Preferred Drug List they are separated out already. They are skeletal muscle relaxants, anti-spasticity and then further down the others are included in skeletal muscle relaxants. I don't know if that's a cause of our previous action or if that's just what preferred list had decided prior.

Donna Sullivan: This is Donna Sullivan. They were broken out in previous meetings by spasticity versus skeletal muscle relaxant activity into these two groups of classes.

Carol Cordy: This is Carol Cordy. There's two medications on this list that we haven't included. I don't know if those are…

Donna Sullivan: That was intentional in the past because the evidence did not show those to be safe… as safe and efficacious as the other products. In the past those drug classes were intentionally left out of the motion.

Carol Cordy: Okay.

Vyn Reese: Maybe we should say skeletal muscle relaxants and drugs used to treat spasticity can be subject to therapeutic interchange. Any other amendments?

Barak Gaster: Sorry. And so I guess we want to say they can be subject to therapeutic interchange within their indicated subclasses? Right?

Chuck Agte: This is Chuck Agte and I would like to ask for additional clarification within the motion because if there are drugs that we are leaving out of the motion entirely I'm concerned about our… whether or not they will be interrupted as part of the class. So if we… if our intent is that they are not safe and efficacious, but part of the class can we say that?

Donna Sullivan: This is Donna Sullivan. It hasn't been a problem in the past that they are considered included in the class, but I'm not sure if you want to make that determination or not. So I think the question you are asking, Chuck, is if one of these drugs that are not listed like dantrolene if it was prescribed would you want it to be interchanged to one of these preferred products? I think that's what… is that the question?

Chuck Agte: Yes, it is and I don't mean to add confusion, but we have… this is one of the older motions originally and we have kind of refined language over the years and there has been interpretation added over time and because we are so detailed in other classes of listing exactly what drugs are in or out of the class that was my concern.

Carol Cordy: This is Carol Cordy. We're kind of doing it with the last sentence in that first paragraph; pulling one drug out. I also did want to change the English on that to say, "It's recommended that it not be covered… this

drug not be covered" instead of "to not be covered". Just some English. But maybe in that same… then after that sentence we should say something about the two other drugs.

Barak Gaster: It should say something like "and is recommended that it not be covered".

Vyn Reese: It is recommended that it not be covered.

Woman: So the committee finds that carisoprodol is subject to abuse and it recommends it not be covered.

Man: It recommends that it never be covered.

Donna Sullivan: The "it" refers back to the committee, not to the drug.

Barak Gaster: That's fine.

Vyn Reese: And we can also say other drugs in this class have not been proven to be efficacious. I don't know if we need to single that out or just leave it the way it is.

Donna Sullivan: I think in the past if I recollect the conversations is that because the FDA has approved these drugs and they are on the market to say they are not safe or efficacious is… we don't want to go there. And that was the reason why we just ignored them or left them intentionally off the list.

Vyn Reese: Okay. Thank you for your historical reference.

Carol Cordy: So if it were… just to clarify then if it were prescribed, one of those other two drugs were prescribed, what happens?

Donna Sullivan: If one of the other drugs were prescribed in… as far as I know that they are subject to TIP and so they would hit up against the edits and then depending on whether or not it's a spasticity drug versus a skeletal muscle drug the preferred products would be listed for the pharmacist to choose from. So what you could say is that the other products that are not listed are… the evidence does not show that they are more

efficacious or more safe than the other products and you choose to remove, you know, make them non-preferred. You could just say… list the ones that are not listed… that we don't put in here as being safe and efficacious. Just spell out like we did with carisoprodol saying, "Carisoprodol shouldn't be covered. These other ones should be non-preferred."

Vyn Reese: Do you want us to add that sentence?

Donna Sullivan: I think that would give Chuck clarity on how… that they're included in the class but are specifically to be not preferred.

Patti Varley: Do we have to say why?

Donna Sullivan: You don't… and now say why. I don't think you have to say why.

Vyn Reese: Do you want to change that around then because… Barak are you still… are you making this?

Barak Gaster: Sure. Somebody else who is making this amendment should describe what sentence it should be.

Vyn Reese: It should be where she's putting it now.

Carol Cordy: I would say the committee also recommends that dantrolene and chlorzoxazone… no… not be preferred but I don't know how to say that.

Patti Varley: Should not be included in the Preferred Drug List?

Carol Cordy: No. They're on the list, they're just not on the preferred of the Preferred Drug List. Be non-preferred? That sounds good.

Barak Gaster: Great. So now should I… I'll read that thing again. This is Barak Gaster. After consider the evidence of safety, efficacy and special populations for the treatment of spasticity I move that tizanidine and baclofen are efficacious and safe for the… For the indication of muscular skeletal relaxants methocarbamol, cyclobenzaprine, metaxalone and orphenadrine are safe and efficacious. The committee finds that

carisoprodol is subject to abuse and it recommends carisoprodol not be covered. Chlorzoxazone and dantrolene should be non-preferred on the Washington Preferred List. Skeletal muscle relaxants and drugs used to treat spasticity can be subject to therapeutic interchange within their indicated subclass on the Washington Preferred Drug List.

Vyn Reese: Is there a second to that motion or any further discussion?

Carol Cordy: This is Carol Cordy. Can I just make a… one little relaxation instead of relaxant? For the indication of muscular… not capitalized, just muscular… musculoskeletal relaxation.

Barak Gaster: And that word should be relaxation, not relaxant.

Donna Sullivan: I'm just trying to make it bigger so it's easier to read.

Jason Iltz: This is Jason. So as I look at the Preferred Drug List the way that it is printed right now, if I was a prescriber I would be a little confused. So I just want to make sure what we've done here helps fix this confusion. Because carisoprodol as you look at the Preferred Drug List has… it says that it is preferred, not covered by L&I and then it says P&T Committee excluded from class. So was that just a…

Donna Sullivan: We have been making changes to the system that creates the PDL for online posting. And it's a rules based formulary or rules based system. So it's automatically making things that are generic preferred. So that… we just need to change the rule. That was an oversight. It is not preferred.

Jason Iltz: So it will show up now as non-preferred?

Donna Sullivan: Yeah.

Jason Iltz: Okay. Thank you.

Vyn Reese: Any other amendments? I'll take a second to the motion.

Jason Iltz: This is Jason. I'll second.

Vyn Reese: All those in favor say, “Aye.”

Group: Aye.

Vyn Reese: Opposed, same sign. It’s passed. I think we should… we’ll adjourn now and we’ll reconvene as the P&T Committee after the DUR discussion this afternoon.

Jeff Graham: Which should be around 2:30.

Vyn Reese: Great. So we’re adjourned until 1:30.

Good afternoon. I want to call the Washington DUR committee to order and we’ll start again with introductions. I’ll start on my left.

Amy Irwin: Amy Irwin, Washington Medicaid.

Chuck Agte: Chuck Agte, Washington Medicaid.

Cathy Williams: Cathy Williams, Board of Pharmacy.

Jaymie Mai: Jaymie Mai, Labor and Industries.

Doug Tuman: Doug Tuman, L&I.

Jeff Graham: Jeff Graham, Health Care Authority.

Ken Wiscomb: Ken Wiscomb, member.

Deb Wiser: Deb Wiser, member.

Patti Varley: Patti Varley, member.

Christine Klingel: Christine Klingel, member.

Susan Rowe: Susan Rowe, member.

Vyn Reese: Vyn Reese, chair.

Carol Cordy: Carol Cordy, vice chair.

Jason Iltz: Jason Iltz, committee member.

Alvin Goo: Alvin Goo, member.

Regina Chacon: Regina Chacon, Health Care Authority.

Leta Evaskus: Leta Evaskus, Health Care Authority.

Donna Sullivan: Donna Sullivan with the Medicaid and Health Care Authority.

Jeff Thompson: Jeff Thompson, Medicaid Health Care authority.

Vyn Reese: This is Dr. Reese. The first order of business is looking at the minutes from the last meeting. Are there any additions or corrections to those minutes I'd like you to bring those up now.

Susan Rowe: Susan Rowe, I have a few. Page 8, last paragraph, line 7 refer should be referral. Page 13, in the last paragraph, line 5 it says nuance and that should say new onset. Page 16, under Patti Varley's quote idiocratic should be idiosyncratic and page 20, under Hurst, line 7 should be pseudoephedrine.

Vyn Reese: And this is Dr. Reese. On page 27, third paragraph from the bottom, it should, as we said earlier it's very important in diseases, not drugs like diabetes and asthma. So it should be diseases instead of drugs in the first line. On the last line it should be a period after drugs and then delete in which and just start new… a new sentence with often. Capitalize often.

Woman: I don't see where you are with that one.

Vyn Reese: I'm on the last line in that third paragraph from the bottom.

Woman: Thank you.

Vyn Reese: So delete in which and then put often in a capital.

Donna Sullivan: Should that be monetarily to buy them or something? To monetarily…

Vyn Reese: It should be monetary access to them. That would be better wording. Any other additions or corrections? I'll take a motion to accept the minutes.

Woman: So moved.

Vyn Reese: And a second?

Jason Iltz: This is Jason. Second.

Vyn Reese: All those in favor say, "Aye."

Group: Aye.

Vyn Reese: Opposed, same sign. The minutes are approved. The first item on the agenda this afternoon is drug… and drug utilization review for Washington is the Avandia restrictions and one of the stakeholders this morning was deferred to this afternoon and it's Long Nguyen from GlaxoSmithKline. He's going to talk about Avandia.

Jeff Graham: And Dr. Reese I want to just say that we're bringing this to you because of the… because of some recent publications regarding this drug and what the implications will be for the agencies because I think there's going to be specific programs really soon for the use of these drugs.

Vyn Reese: So we'll hear this stakeholder input and then we'll go ahead and start with the discussion after that. Go ahead Mr. Nguyen. I don't know if your microphone is on. Maybe stand closer to it.

Long Nguyen: Hello?

Vyn Reese: That's better.

Long Nguyen: Thank you for the clarification this morning. Again, my name is Long Nguyen and I'm a PharmD representing GlaxoSmithKline here to discuss the latest Avandia announcement by the FDA. As most of you are already aware on September 23rd the FDA made a decision regarding Avandia and all Avandia pertaining products. The FDA announced that all Avandia containing products will remain available on the market, but with additional safety labeling and restriction of use. And they have requested GSK to draft and develop a REMS program for use of Avandia. And so… and the details of the REMS program has not been available because we're still… have to develop the program and present it to the FDA for approval and implementation. So unless the committee members has any questions in regard to the FDA announcement, my presence here is to address any questions or concerns that the committee members have. But also I would like the committee to consider that because the details of the REMS program have not been established. That the committee consider making no changes to the Avandia status until more information is available.

Vyn Reese: Okay. Thank you. I don't think we'll have any questions right now, but after the presentation we may, in discussion, may have more.

Long Nguyen: Sure.

Vyn Reese: We'll reserve the right to recall you if we have additional questions. Okay?

Long Nguyen: Absolutely. Thank you very much for your time.

Vyn Reese: Jeff, do you want to give us some more background information?

Jeff Thompson: Well, I think this information was published, as he said, in late September regarding the findings of probably increased cardiovascular problems with this drug. And I know we've had these questions in the past, and have not really come to… we didn't make any decisions regarding limitation of this drug for our patients. And so we just brought it to you to see if you have thought of… or if you have any recommendations for us at this time for this drug class. We will be reviewing this drug class in December, but we didn't have the materials ready for you at this time.

So we could leave it as it is, we just wanted to make certain that you were aware that we were…

Vyn Reese: I think we made Actos the preferred…

Jeff Graham: No. We actually left both of them…

Vyn Reese: Yeah, both of them are preferred. So we didn't make Actos the preferred drug.

Donna Sullivan: This is Donna Sullivan. I think you said that Actos had to be on there.

Vyn Reese: Right. We said that Actos had to be on the list.

Donna Sullivan: But our… based on that decision right now they are both preferred because I believe at the time the cost analysis Avandia came in as a less expensive product. So we would like direction on whether or not we should keep Avandia preferred or make it a non-preferred product or to put further utilization controls on it for Medicaid. Require prior authorization for it.

Susan Rowe: This is Susan Rowe. So if… tell me… if a physician writes for pioglitazone and then is it also preferred? Does it have equal status with rosiglitazone?

Donna Sullivan: Yes, they are both preferred right now.

Patti Varley: This is Patti Varley. I'm just curious. I'm assuming this finding that was… came out and was published at the point of sale is now discussed as part of the patient safety information with the patient at point of sale. Is that true or not true and that prescribers now having this information…

Donna Sullivan: I have a question and that might be back to the gentleman that just spoke. If the REMS criteria is not fully developed yet has anything changed at the retail setting or are those prescriptions just being filled as written? Other than the publication that providers might be, you know, bringing patients in and changing them I don't know if there is a stop at retail.

Long Nguyen: At this time because the FDA announced that Avandia products still maintain on the market until the REMS program has been approved we are not actively promoting Avandia because there will be some significant labeling changes. However, because the FDA still maintains Avandia on the market, patients who are currently on Avandia and new patients who their physicians believe that they should be on Avandia, can still get Avandia.

Vyn Reese: This is Dr. Reese. As I understand it, it was taken off the market in Europe. Is that correct?

Long Nguyen: That is correct, yes.

Vyn Reese: I mean there are grave safety concerns given cardiac risk in a group of patients that's already very high risk.

Long Nguyen: Yes. And um…

Vyn Reese: And that's why it's a very serious side effect. It looks like it's been proven in… almost fairly certainly that that's the case, especially against its comparator drug. So that's a very grave concern and it's, you know, I personally am not prescribing it anymore and I'm taking all of my patients off of it and switching to the other drug in its class. So it's… I think it's a grave concern.

Long Nguyen: Sure. Absolutely. And if I may make an additional comment. Part of the September 23rd decision that the FDA announced, they also required GSI to have an independent organization to re-adjudicate the end points from the records study. So they do request the re-evaluation of that trial which was the Avandia cardiovascular outcome trial. So I just hand to make sure that that was part of the announcements as well.

Donna Sullivan: So this is Donna Sullivan. To get back to Patti Varley's question, I think at this point in time there is nothing to block Avandia from being filled at a retail pharmacy if they are currently on it or a prescriber chooses to start it in a patient. So unless a doctor is actively bringing in their patients and switching them to a different drug, then patients are continuing to go

through and get treated with Avandia because the REMS program is not in place. So we would like to know, could you give us some direction to implement some either prior authorization or, you know, give us some guidance on how we could maybe restrict the use at least in new starts on Avandia and then how to address currently the patients that are on it.

Carol Cordy: This is Carol Cordy. It sounds like part of this is an educational piece and if it were prior auth the physician who prescribed it would be talked to and educated.

Donna Sullivan: Yes.

Carol Cordy: So I think that would be a good way around it.

Donna Sullivan: So could we get a motion or some guidance one way or another.

Vyn Reese: This is Dr. Reese. The key thing is you want to stop all new starts for sure and you… it's hard to know what to do with patients who are already on it. Just stop refilling it and then their diabetes goes out of control. So it's like… it's a difficult situation. So we need to discuss that a little bit.

Deb Wiser: This is Deb Wiser. With therapeutic interchange I would think that pioglitazone could be used as the interchange for Actos at least to handle the short-term issue of people still being on this medication. Also I think setting non-preferred is not part of the committee issue, but just saying… I mean making a prior auth is not a committee issue, but saying that it's non-preferred would be something that the committee could do.

Donna Sullivan: So this is… you're wearing a new hat today or after lunch. I misspoke earlier by saying make it non-preferred. As the DUR board, which we are convened as right now we… the authority would be to authorize us to put in some prior authorization criteria. So if we have the current users or the current patients on there we could send out letters, you know, summarizing the FDA's action and letting them know that as of a certain date the drug will not be covered or will require, you know, special authorization to continue it and then give them time to switch over to either Actos or another product. And so if you, you know, give us some guidance as far, you know, what you would like us to do for the current

patients as well, you know, I think, you know, Dr. Reese you said potentially, you know, stopping it for new starts that would be helpful as well.

Patti Varley: This is Patti again. Can you clarify if we sent those letters to the clients who are receiving… can we also send that same letter to prescribers?

Woman: No, it should be sent to the prescribers.

Donna Sullivan: I think it will be sent to the prescribers I believe.

Patti Varley: I thought you said to the…

Donna Sullivan: Well for us… for uniform medical plan we would probably send it to the patients and then, you know, relay on patients also to take it up with their doctors as well.

Patti Varley: Right. And I guess I heard to patients and I'm just thinking could it go to patients and prescribers because some of the patients will get that letter and not necessarily be knowledgeable enough to know what that means and really the point of prescribing is with the prescriber.

Donna Sullivan: I'm sure we could do it with both.

Ken Wiscomb: Yeah. This is Ken Wiscomb…

Chuck Agte: As far as any role as the DUR board we will take back whatever recommendation for Medicaid that you supply. So if you want it to go to clients we would do that. If you want it to go to prescribers we could do that. If you don't want it to be letters and you want it to be active PA involvement we can do that. Whatever you think is the best course we can move forward with. On the topic of letters, our prevailing philosophy in the past for Medicaid clients has been whenever possible we provide the information to their prescribing physician because there is precedent within Medicaid, not within our state, but there is precedent out there where communication to clients has been misinterpreted and people have quit taking medications that they should be still on. So we try and keep our communication to the prescriber whenever possible. But if

you… but we'll do whatever it is that you think is the best course of action.

Ken Wiscomb: Ken Wiscomb. Just for clarification did I understand you before to say you need some direction from us to stop new starts?

Donna Sullivan: We need a formal recommendation on how to handle Avandia going forward for new starts as well as existing patients. We… at this point in time for uniform medical plan, because it's on the Preferred Drug List and it's a preferred drug we would either need to convene as the P&T Committee to say, "Make it not preferred," or as the DUR board you can just tell us to make it a prior authorization type of a product for Medicaid.

Susan Rowe: So Susan Rowe. I have a question. It's been my impression that most physicians have chosen pioglitazone kind of as new starts, but I'd like to know, do we have any data? Are there continuing to be an even number of new starts or do we have that data?

Donna Sullivan: We don't have that… we don't have that data right now. I can't tell you off the top of my head. I would imagine, like you said, most likely because there's been so much notification and publication about the issues with Avandia that a prescriber would not start it, but it would just, you know, give that extra protection that it's not going to happen. Go ahead.

Cathy Williams: Cathy Williams, Board of Pharmacy. I just have a question. Has GSK sent out a "dear colleague" letter to all prescribers in the country alerting them of this… of these new findings and imminent steps to maybe take it off the market?

Long Nguyen: Yes. We… since the announcement we have sent out letters to all physicians letting them… aware of the announcement and the next step of GSK is to develop the REMS program and more details will come as soon as it is available.

Donna Sullivan: When do you expect the REMS program to be in place?

Long Nguyen: The FDA requested that we, GSK, respond back with a draft protocol of the REMS program for review and approval 60 days after the announcement. So we're looking at late October… late November.

Vyn Reese: This is Dr. Reese. I think that we should just instruct you to stop all new starts and send a letter to the providers for sure. And then I don't know if we do a therapeutic interchange and if we have to do that this afternoon; we are going to be reconvening as P&T this afternoon. If we can talk about a therapeutic interchange then. So is that… would that still be under our current hat as DUR? For safety reasons stopping new starts and sending a letter to providers? I got the letter from the manufacturer too and that was very helpful. The snail mail isn't 100% and I'm sure people are prescribing by habit still and it could still be ongoing. So I think we should… we should be certain that we do stop new starts and that we talk about a therapeutic interchange when we reconvene.

Donna Sullivan: So I believe… this is Donna Sullivan again. I believe I'm Donna Sullivan… that as far as the new starts that is a… I think a DUR board decision. As far as a therapeutic interchange if you want to make it subject to therapeutic interchange then that is a P&T Committee decision and Jeff you look like you want to say something. So were you going to interject?

Jeff Graham: No. I was just going to ask if you could tell a provider all their patients that they have on the [inaudible]?

Chuck Agte: Yes. It would be… it wouldn't be something that… this is Chuck Agte. The nature of the question kind of threw me off because if they called us up on the phone, no. If we do a data pull to identify all clients and all prescribers we can provide that information.

Alvin Goo: This is Alvin. I think the [inaudible] in the classes is a very attractive class, theoretically. But evidence wise I'm not too sure it's any better than what we have as far as oral hypoglycemics. So I would not want to do a therapeutic interchange and promote continued use of these agents. I still think there's a lot that we don't know about them and I would just caution not to do a therapeutic interchange.

Vyn Reese: I agree totally with you. The question is if it's that or nothing. If we stop… if we restrict Avandia and say they can't get it anymore what do they do? And they may have already been tried on two other oral agents and that may be the third one and they may already be out of control. You don't know any of that. So when you try to restrict it it's going to be tough to do.

Alvin Goo: Right. Yeah, but I just don't want the interchange to happen at the pharmacy. It should happen with a discussion with the provider.

Barak Gaster: Yeah. This is Barak Gaster. I would sort of come back to my recommendation from the DUR committee that we would recommend prior authorization for Avandia.

Deb Wiser: This is Deb Wiser. I think you were also looking for a recommendation regarding how to communicate is my impression. So then I think a letter to the physicians…

Vyn Reese: A letter… a letter.

Barak Gaster: We would recommend prior authorization for Avandia as well as a letter to all providers notifying them about these concerns and the impending start of prior authorization.

Vyn Reese: That would be no new starts then essentially is what we're saying without prior authorization.

Carol Cordy: This is Carol Cordy. Even for refills… those would be prior authorization too? I mean there should be a way that even refills get that call.

Chuck Agte: Whatever you guys decide we can make happen.

Barak Gaster: I would say prior authorization, period, whether it's a new start or a refill.

Donna Sullivan: So no grandfathering?

Barak Gaster: Right.

Donna Sullivan: Okay. So what we would do to the most extent, Jeff, we would work on drafting a letter to the providers and send it out at least 30 days before we're going to make the decision to give them time to potentially either contact a patient or bring them back in for an appointment and make those changes. So we'll get that worked out.

Barak Gaster: This is a drug that was a hair's breath away from being taken off the market completely. So I think a prior authorization is absolutely appropriate.

Deb Wiser: This is Deb Wiser. With that… I think the question is whether that letter would be including the list of patient names that the provider's actually have on Avandia. Because if it's a generic letter it may not flag to them who to contact.

Chuck Agte: We could take a couple of approaches. If we… in moving this to full PA one standard step for Medicaid is as notification to pharmacies to expect the change we would publish the change in a memo at least 30 days in advance and then in addition to that we could also do a letter to physicians and we can include in that, if your recommendation is that it be a single letter detailing all their clients, we can easily do it that way. There is also the fact that even if we do a letter warning in advance then the actual… if we're going with the full PA stop then they will receive additional communication each time they're actually trying to prescribe it for someone.

Vyn Reese: So let's make that in the form of a… this is Dr. Reese. We need a motion. So maybe you can just read back our thoughts here. So basically we're going to require prior authorization for Avandia. We're going to send letters to all providers in Medicaid regarding Avandia including their list of patients on Avandia. And that's going to be our current action. Okay? And we can do that as a DUR board.

Donna Sullivan: That's what I have. Yes.

Vyn Reese: Then we don't have to worry about any of the other stuff.

Donna Sullivan: Right.

Vyn Reese: Okay. So that's the motion in… for the committee. So is that right, Barak? That was your motion? Jason, do you want to add something to it?

Jason Iltz: This is Jason. Just a couple of things. The first question I have is regardless of all the letters and things there's going to be somebody that falls through the crack and comes to the pharmacy for this refill and all of a sudden PA is required. So is there a way at the pharmacy level if somebody does fall through the crack to allow a one-time EPA override or something like that just so that they can get a 7-day supply, 14-day supply, whatever it may be, if they fall through. That's my first question and then the second thing I just want to pose to the board is, you know, I have concerns about the class as well. So my question would be for all new starts should we require prior authorization for either one of the medications, not just Avandia? But I'll let Chuck answer while the board ponders that other portion of it.

Chuck Agte: The… how we would normally address the need for a one-time fill is our emergency fill provision. In general, the pharmacy should be contacting us for PA. If there is some reason that they were not able to contact us for PA in a timely fashion, our emergency fill provision is always in place and if they feel the client must have the drug prior to receiving an authorization decision from us, all pharmacists are authorized to dispense and let us know after the fact what they did as an emergency fill and we will approve it. So that's kind of our standard fail safe for any situation like this for any drug that's going on to PA. That option is always there if the pharmacy can't get an authorization decision in time for one way or the other. We also have standard provisions of continuation of benefits. So if it is a refill for someone when that first PA call comes in we are required to go ahead and give them an additional fill. So it would be a stop. The pharmacy would get the rejection. But as long as the pharmacy contacts us if it is a refill the client will automatically be authorized for one fill while we make the decision on future fills.

Ken Wiscomb: This is Ken. Jason, I'm not sure I disagree with you but it seems to me it would make more sense to take this action about Avandia because it's

prompted by FDA action. And if we're going to take action against the class then we should do that in December when we do the class review.

Vyn Reese: This is Dr. Reese and I totally agree with what Ken just said. This is an emergency situation. Actos doesn't share the cardiac risk and as a fourth line agent it might be indicated in some patients and we can discuss that after the full review in December.

So the motion in front of the committee, if you want to read it back one more time.

Donna Sullivan: This is Donna Sullivan. So the recommendation is to place Avandia on prior authorization for new and existing patients with the idea of stopping or preventing new starts and that Medicaid will send letters to doctors as appropriate within 30 days of making the change.

Woman: With the addition that the letters will contain the list of patients…

Donna Sullivan: Yes, yes.

Patti Varley: And for point of clarification it should be provider and not physician because there are other prescribers.

Donna Sullivan: Yes.

Vyn Reese: Okay. That's the motion in front of the DUR. Is there a second?

Ken Wiscomb: This is Ken Wiscomb, I'll second.

Vyn Reese: All those in favor say, "Aye."

Group: Aye.

Vyn Reese: Opposed, same sign. It's approved. Now let's move on to the next item on the agenda. Jeff Thompson is going to be talking about the MPA generics first for new starts and AAPs.

Jeff Thompson: So this is Jeff Thompson. Let me start with just a clarification from your discussion this morning on the preferred status of all the atypicals. What I have up on the screen here is the current expedited prior authorization criteria for all of the injectables except for Sustenna. And what I would like to do is suggest that we maintain these EPA criteria for consistency so people aren't just starting on the injectables. And this has been working. I don't believe I've heard too many complaints about the EPA criteria at this point. Chuck?

Chuck Agte: No. We have not had any consistent or significant complaints that I'm aware of in regard to the expedited criteria on the injectables.

Jeff Thompson: And this would maintain the FDA indications for the injectables and we would do the same for the one drug that's not up there and just produce these. And that would be at the pharmacists discretion to actually, you know, make sure that the FDA indications are being followed for the injectables.

Vyn Reese: This is Dr. Reese. I don't believe we changed that this morning.

Jeff Thompson: When you made them all preferred my interpretation of that is all prior authorization and EPA come off unless I can talk to you about an EPA or a safety issue or some other, you know, I mean that's the way we've usually been handling it. And with this drug class I think we just want to be absolutely crystal clear.

Donna Sullivan: This is Donna Sullivan. I think we've gotten guidance to keep the injectables on our… on EPA for FDA approved indications. So we wouldn't be removing the EPAs on these products. We would just be adding the Invega Sustenna, take it off of prior authorization like it is right now and then just adding it to the EPA program like all of the other injectable atypical antipsychotics currently are for the FDA labeled indications.

Vyn Reese: This is Dr. Reese. That was our intent. I mean…

Jeff Thompson: I think… I think what I just talked to Duane… I just want to make very clear if you could just vote that these criteria and then criteria defined for

Sustenna would be developed and would be continuing as far as the preferred drug list pertains to antipsychotics.

Vyn Reese: That's our P&T… can we do it here?

Jeff Thompson: No. This is EPA criteria… you can do this here. This is EPA criteria.

Vyn Reese: Okay. If we can do this here, great. Okay. There's a motion that we apply EPA criteria to all the injectable atypicals. I'll make that motion. Is there a second?

Barak Gaster: Barak Gaster, I second.

Vyn Reese: All those in favor say, "Aye."

Group: Aye.

Vyn Reese: Okay.

Jeff Thompson: Just one question Duane wanted to make sure we were clear on this.

Jeff Graham: Jeff, this is Jeff Graham. I have a question. Why is it we heard so much this morning on problems getting these drugs through? Is that because they don't know the EPA criteria?

Jeff Thompson: No. I…

Donna Sullivan: This is Donna Sullivan. I think what the people were talking about was Invega Sustenna because it had not been included in OHSU review. It was actually on a hard PA and we admit we are behind on getting some of those approved. So now that criteria will be removed and we will get it onto EPA where that should no longer be a problem.

Vyn Reese: So, yeah. That should take care of the problem that we heard about this morning.

Jeff Thompson: That will take care of the problem.

Vyn Reese: Right. Yeah.

Jeff Thompson: They will be consistent with the same criteria that we have posted here based on the package criteria.

Vyn Reese: Okay. Now you can launch into your discussion.

Jeff Thompson: So, again, this is Jeff Thompson. So just an FYI November 1st we are going to begin the generic starts on new/naïve clients for both children and adults. We've actually been doing children since last March…

Chuck Agte: Last October.

Jeff Thompson: Last October. Okay. How time flies. And so one of the things that we've been doing in the Mental Health Drug Workgroup is we've come up with the criteria, we've been publishing that criteria. I've been on the road show, I've talked to NAMI, I've talked to the Mental Health Clinic Association, we've given all the materials that are in your handouts here to anybody and everybody that has asked and we're relying on the drug companies, the associations, the providers to share this so that everybody knows and has sort of a very good knowledge of what the myths and legends are for generics, some explanation both at the provider and the client level on what Generics First is and is not, and then in addition to that we've done the broadcast facts to the pharmacies on the EPA criteria, which are consistent with the principles that we worked at with the Mental Health Drug Workgroup. So this is more of an FYI or just to hear any comments, suggestions or concerns. But we've been on the road, you know, publishing this, telling people about it, but it will happen November 1st. So any client who comes in with what we identify as a new start we will ask that prescriber to start the generic risperidone first or they will have to explain either why it's not a new start, because we don't see other drugs that have been prescribed or they fit the criteria that is in this document.

Vyn Reese: Any comments from the committee? I think we've gone through this before. We do have some stakeholder input from…

Barak Gaster: I just have a quick comment. This is Barak Gaster. And this looks great. It's really clearly written. It will be useful information for people and this will probably come out in your ordinary copy editing process, but I would just draw attention to the issue 3, the DSHS Pharmacy News Issue 3, the Roman numeral 2 Q&A. The second question, "What are the principles around AAP new starts when the brand is a better choice?" And it's that very first bullet point does not read clearly. It seems like the… seems like there is a missing word in there or something. I'm almost wondering whether that very first bullet point really shouldn't even be a bullet point. That it's more the lead in stem to the bullet items that are below it, or something.

Vyn Reese: Where are you exactly?

Jeff Thompson: It's actually… the "of" is actually… it looks like we need to move the "of". It's actually a continuation up there. We can correct it.

Barak Gaster: Okay. I'm just calling that out to you that I didn't understand…

Jeff Thompson: I'm seeing a wayward parenthesis in there too.

Deb Wiser: This is Deb Wiser. Also in bullet four…

Jeff Thompson: You can directly hold Chuck responsible for that editing.

Chuck Agte: There you go.

Jeff Thompson: He's actually a very good editor. So we'll make sure that everything else is cleaned up; where I am not.

Christine Klingel: This is Christine Klingel. I just actually want to commend the work that you've done and with your committee. So far the information that I've seen that has come out on this has been very thorough, very complete. I've been educating some of the physicians at our clinic and they seem to understand it. So I think so far just from personal experience so far… I mean we'll see what happens November 1st, but I think the work that has gone into it has been very thorough and very complete. So I want to commend your committee on the work that you've done so far.

Barak Gaster: I second that.

Vyn Reese: And we want to maybe have a general committee commendation for your work. So appreciate it.

Jeff Thompson: Thank you. I appreciate it. So Chuck, Amy, November 1st everything is loaded and ready to go. I think we're going to do one more broadcast fax on the EPA criteria. We're planning on that?

Chuck Agte: Yes. We've sent out the… our standard practice for our memos is they're published 30 days in advance of anything going into place and then the week prior to the change we send a fax out to all of our participating pharmacies with a copy of the memo just as a reminder that something is about to happen. On this particular effort because of the sensitivity of the drug class in question we've already broad… we broadcast faxed our memo at the beginning of the month. It went out again on the 18th and it will go out during the last week of the month next week.

Vyn Reese: Okay. And I believe Dick Miyoshi wants to speak.

Dick Miyoshi: I'm Dick Miyoshi from Harborview and Mental Health Workgroup. We've worked pretty hard on the Generic First trying to think of ways that it wouldn't work and as far as I can tell on new starts we've covered just about everything. I mean the… I swear the CATIE All Cause Discontinuation is restrictive compared to the way we've written this thing. So that is our first part. This next part we're working on is the adherence part which may or may not be… have more to do with the injectables, which are not inexpensive but do help with adherence. And we've worked really hard and Jeff has really worked hard on this and that's about all I'd like to say. Any questions about the process or…

Vyn Reese: Thank you. Are there other stakeholders that would like to speak?

Helen Nilon: Yes. I would like to speak since I spoke inappropriately this morning.

Vyn Reese: That's okay. You were on target. We were discussing it twice under two different headings.

Helen Nilon: Oh Okay. My name is Helen Nilon. I'm here to speak on behalf of the Community Transformation Partnership or CTP. The CTP is an organization of consumer organizations which represent over 100,000 individuals in this state. Some of our members are Mental Health Action, Consumer Voices, or Born Passages of Village Project II, NAMI Washington, Word Bridgers, WADADS, PAVE and others. We're here today to urge this board not to continue… not continue with fail first policies which we believe hamper the recovery of most individuals. We base this, in part, on our own experiences and upon comments that Dr. Thompson made to the P&T several months ago when he proposed that Generics First have naïve individuals experiencing a psychotic episode be given risperidone. As we expect these individuals to "fail" so why not start on the cheapest drugs. I don't know if you all heard that, but I heard it crystal clear and was shocked.

Vyn Reese: That's not correct. I would… that's…

Helen Nilon: What did you hear him say?

Vyn Reese: I heard that you should be started on Generics First because all the antipsychotics… we don't know which one is going to work. You don't expect the risperidone to fail, you expect many of them will fail.

Helen Nilon: My understanding is that we expect many…

Vyn Reese: He didn't say that.

Helen Nilon: …of them to fail in addition to risperidone.

Vyn Reese: The fact is that, you know, a lot of them fail the first time and you have to try a second agent. But for a naïve start for someone who has never been on it before, but we're talking about starting risperidone as the first drug you try and it may be one of many. That's all we're saying in that. So I think you need to make sure you're on target… is this the same thing you said this morning?

Helen Nilon: It's not.

Vyn Reese: Okay.

Helen Nilon: No. But I do, as you notice probably, take notes and put things in quotes. When they're in quotes… I don't do this for my memory of that day although I remember it, but I have it in quotes in my notes. We know that all medications are not the same even within a certain class such as we find within antipsychotics. Tremendous research was done in the 90s to understand the brain and chemical interactions within it. Due to this research much newer medications have been brought on the market and have been tested. We also know through national studies been done by the National Institute of Mental Health and others that when choice is taken away from individuals, that costs rise. With this policy we, meaning Washington State, will see an increase of ER visits, hospitalization, the judicial system and jails. During this time of severe budget constraints it does not make sense for medication to shift costs to other governmental services. The human toll and suffering that will be experienced is unacceptable. Please focus on choice between the parent… patient and their doctor, which we call Recovery First and do not support generics as a policy first. Thank you for consideration of this request. Any questions?

Vyn Reese: This is Dr. Reese.

Helen Nilon: …other than that one comment?

Vyn Reese: Any questions or comments from the committee?

Patti Varley: This is Patti Varley. I just have a comment. In any drug class what typically happens is that there are initially some initial medications that are developed and for FDA approval in the sequence from there out any new medication within a class for FDA approval has to prove it is better than placebo. We don't have a system whereby the requirement through FDA is that a second drug or a third drug or a fourth drug or a fifth drug within any class has to prove that it's better in efficacy or safety than the first drug in a class.

Helen Nilon: Uh huh.

Patti Varley: That's a drug development problem that goes beyond any of us in this room can control. That being said the other thing is that a lot of the older drugs have longer and better track records than newer drugs in regard to safety and efficacy because they've been used longer and we have more information about them. And to your point, and I don't have Jeff's quote so I can't say yes or no to it, but what I can say is that all of us who are selecting within this class for a treatment naïve patient there is little to no guarantee that any particular one on first choice, whether it's the cheapest or whether it's the most expensive, is going to be the right fit for that patient. And I think that that is where that particular issue comes that for most patients you have to try something. You need to clinically evaluate it and you need to be able to make appropriate clinical decisions for that patient based on that response. But there is no evidence to date that within this class, and many others, that there is a definite algorithm or predictability about which one is going to be the right one for an individual patient. So just to clarify that point I think your point's well taken, which has never been the intent, which is that if something is tried and doesn't work whether it was the cheapest or the most expensive, the idea was that you would go from there to try yet another for that patient to make sure you got best clinical outcome and when the unknown is there and we're trying to keep resources available for as many, and more are coming, I think doing it in a conscious way and I would argue that in some cases your advantage to an older drug, which now is cheaper is that evidence base that you've got over time that you don't have as much of with the newer agents.

Helen Nilon: I agree with what you said other than that there's no information available. I know on Tuesday or Monday I was at NAMI Greater Seattle, one of 24 affiliates of NAMI where Jeff presented information regarding non-adherence to medications—antipsychotics. And I specifically asked if I could have a breakdown of which antipsychotics do people not adhere to. Because that's our problem. People stop taking their medication for typically a reason. Jeff indicated that information was available…

Patti Varley: Your point…

Helen Nilon: We don't have it yet.

Patti Varley: Your point though is well taken, which is adherence versus efficacy are different. They are different issues.

Helen Nilon: Right. And if someone won't take a new medicine because of severe side effects then it's not effective or adhered to.

Patti Varley: And predicting what patient will have what side effects on what meds is also very difficult.

Helen Nilon: Correct. Correct. We don't know that. I will concede that.

Donna Sullivan: This is Donna Sullivan and in that instance if a patient were to stop the drugs there's… the criteria here is that, you know, if the patient stopped their drug because of side effects that then a brand would be approved for that patient. So we're not saying that you can't say it, ever. It's just that if you're going to start it, start on the least costly drug, which is the generic right now and if that one doesn't work over time the patient can then… might move to the brand name products without further cri- prior authorizations.

Ken Wiscomb: And as I remember during our discussion we asked Jeff, "Do you literally mean one pill?" And he said, "Literally one pill. If they take one pill and they have a side effect they can go on to whatever they want."

Chuck Agte: This is Chuck Agte and I wanted to speak to some of the work that Dr. Thompson and the Mental Health Workgroup have done and in that good work that they've done they have protected client choice because one of our criteria that can be applied at the pharmacy level is that if the prescriber has had a documented conversation before prescribing the brand name drug where he has had that conversation with the patient about whether or not risperdal is the right drug for them, or risperidone, that if there's documentation that he addressed that difference between the generic and brand and talked to them about it and they said, "I will not take that drug for whatever reason." As long as the doctor has had that conversation with the client then they do have the option of prescribing something different.

Helen Nilon: They do and I think with additional pressure on doctors to write the generics that it's unlikely that those doctors are going to be writing non-generic drugs when there is pressure. But I do appreciate all your comments, thoughts and we'll continue to follow.

Vyn Reese: Okay. Thank you. And could you identify yourself, please. You're a stakeholder?

Farrell Adrian: Yes. I'm Farrell Adrian. I am the new President of NAMI Washington. I represent thousands of family members and people living with a mental illness and we are adamantly opposed to this decision. We just feel that balancing the budget on the backs of our most vulnerable citizens is horrible. I personally have taught about 200 family members, our family-to-family class and I see again and again that for so many of our families their family member refuses to take medication. I personally know about risperidone in that my son's first drug was risperidone and it gave him terrible tardive dyskinesia and did not manage his symptoms both positive or negative very well at all. And eventually after the tardive dyskinesia got so bad he was put on another drug. It took many, many months for that tardive dyskinesia to go away.

The other thing that is especially concerning to me is that it is so hard to get our family members to take a drug in the first place. And if they take one that has those kinds of side effects I think it's less likely they'll be willing to take another drug. So it's very good and well to say if this person says, "No," but that is pre-disposing an incredible amount of sophistication that we all know here does not exist with our family members.

I really believe that you'll see, you know, many more criminal justice problems, many more hospital visits. This isn't going to end well I'm afraid for all of us. So I ask you, all of you, to consider success first to allow the doctor the choice, not fail first.

Vyn Reese: Thank you. Are there questions from the committee or comments?

Diane Eshenbacher: Thank you for the opportunity to speak to you today. My name is Diane Eshenbacher. I'm a registered nurse from Spokane, Washington and I'm

here on behalf of the Mental Health Planning and Advisory Council and actually some of the comments that I was going to say today shifted a little bit when I heard some of the conversation you had here in regards to… I think the paperwork that you've done, the explanation for Generics First is very good. We did have some concerns that there wasn't going to be a mass mailing or notification of the public… we didn't understand was this going to be a passive process or like if somebody showed up and they asked the pharmacist, you know, "Hey, why did they switch my medication?" or was this going to be an active process where they would be talked to and counseled on the changes that were happening and we really didn't understand which it was going to be. But I think something that pops into my… now having heard you speak and talk about efficacy and failure is that perhaps there needs to be a little bit more explanation or at least a little more comfort given to the community that you're serving to know what is failure first, because failure is a very negative word, obviously. And I guess a lot of… to the consumer community it kind of brings to mind, you know, is it that you've been calling and calling the doctor saying, "You don't feel, you're not sleeping," you know, they are running down the street in their underwear or something and they end up back in the hospital versus that, "I took the med," you know, "I got it. I took my first dose. It doesn't agree with me. I was restless, I'm not doing good." And it's going to be changed. What we got from the idea of failure first was that you had to have this big catastrophic failure on it. So from my perspective it's changed a little bit but, you know, I try to keep in touch with my consumer community and if I'm not getting that as what constitutes a true failure then obviously they're not getting that either. Thank you very much for the opportunity to comment.

Vyn Reese: Thank you. A couple of clarifications. This is Dr. Reese. Is that, you know, your idea of failure first is what's in here. If the patient has a reported side effect that's a failure or it's a contraindication of that drug and if they call the doctor and say, "I'm having this side effect," the doctor is supposed to change the drug and that's in here. Also there's a lot of good, you know, carefully written verbiage here to protect the patients. If they've had a drug before like this then they can't start it again. We've reviewed this extensively; all the antipsychotics they all have a different product… they have a different set of side effects. I've had patients that have been on olanzapine with… that developed

diabetes and were seriously ill because of it and a massive weight gain, 30 or 40 pounds in a year, where their health was impaired. So each drug is a little different and some of them are equally devastating. So with any of those side effects they should be taken off that drug and put on another one. Clozapine causes agranulocytosis, which is fatal and that's why it's restricted. It has the best adherence rate though for… or best effect in this. So it's the most effective drug and that's what… but reserved because of its serious toxicity. So these drugs are all… none of them are without serious side effects and the side effect ratio may vary between EPS and weight gain and metabolic syndrome and diabetes and if they are all in that spectrum somewhere and if one has more of this one and less of that one and they're all bad as far as that goes.

So we have to individualize the drug for the patient and make sure if the drug isn't working for the patient or they have a side effect to the drug they get another drug and that's what… why this is crafted. And it's clearly a matter of resources, too. Because if we don't do this we will be able to cover fewer patients who are mentally ill. That's the truth and they are talking about stopping all medications totally if there is a huge budget cut, which is going to be devastating. So if you want to really put your, you know, your energy into something it's to stop that proposed cut in all Medicaid drugs. It's a very complex problem, but this is a sensible step. Nobody knows… this is the honest truth, of which one of these drugs is going to work for a patient. And the only way to do it is to try… if you've had a personal side effect to risperidone you're going to think that is the most horrible drug in the world. I don't want anybody to ever have that. Or if you gain 30 pounds on olanzapine you're not going to ever want to start that drug on anyone. But that's just one side effect of lots of side effects. That's the key thing and we've really tried to craft this and the committee… the committee's… Jeff Thompson's work on this has been outstanding to look at all the possible… and all the people that have worked with him on this. To look at all the possible ways in which we can protect patients. Okay? And that's the idea is to protect patients from side effects and from drugs that don't work and that's why we've gone through this exhaustive process. So thank you.

Woman: Can I respond to that real quickly? Yes, the document is excellent. I read through it. I think it's something that most people will understand.

Although there's always, you know, that curve as far as when you're dealing with the public as far as their ability to understand this kind of information. But I, you know, that helps to know… I'm wondering is the prescribing community in that frame of mind too of what constitutes failure first? That if even something so simple as one symptom and you get to change is that. So it may be kind of… there's… there's some learning with it.

And please also note that… the impact… we are aware of the potential that they may go… that we may lose prescription coverage and we are incredibly concerned and trying to gear up so that should something like that happen that the consumers will be well represented and the best decisions will be made on their behalf. So thank you very much.

Vyn Reese: Thank you.

Farrell Adrian: I'd like to say just one last thing and that is the two times my son's medication has been changed have both led to just hideous experiences for him and for our family when they were making that change. And in one case he ran into someone who had cocaine and started using cocaine and we went through all sorts of drug treatment, which cost our State of Washington a pretty penny. And it was about a two-year process to get him back on track with that medication change. I know I'm speaking very personally. I know I've also been sort of grumpy and I'm usually not that grumpy and I'm glad to meet you all and we'll probably see each other again. I probably won't usually be this grumpy, but it's pretty personal. So thanks.

Vyn Reese: Thank you.

Ken Wiscomb: This is Ken Wiscomb and I think I'd want you to know that, you know, everyone here is certainly sympathetic with the situation you experienced with your son. I think the bigger picture that we try to look at is if you sort of think of that pie of social services that's available for not only prescription drugs, but for mental outpatient… outpatient mental health programs and retraining programs and all those social services things. If we can take money out of this little piece of the pie because of what we find to be clinical evidence that we can do so without

causing harm and we can shift it somewhere else we can help more people. We've spent a great deal of time looking at the gaps that you spoke about between where people are in Harborview or in primary care clinics and they get stabilized on one atypical antipsychotic and then they get lost in the system and they're unable to find a mental health provider or they're unable to get a prescription refilled and then there's this gap and sure enough they end up back in King County jail or some place. So we understand that that's expense. But the bottom line with these medications is there's less than a 50%, there's less than a 40% chance that people are going to find total remission with these drugs. It's not the fault of any one drug, it's that no drug in this class works effectively for everybody or even more effectively than perhaps 40% of the time.

So all we're really trying to say is, given that, if there's… there's more than that, but say there are five drugs and we know all five of them work essentially exactly the same the odds of it working the first time in one person are exactly the same. Why not ask people to use the cheapest one first with the chance that it might work? And if they take one pill and they have one side effect then they can go on and use whatever drug they want.

Woman: As a family member with 17 years experience, what it seems to me is that we are on a slope that year after year my child's services are cut and people nicely tell me why that happens and they promise that they still have my child's best interest at heart, but the fact is it gets smaller and smaller and smaller and that's what we face and that's why we [inaudible].

Ken Wiscomb: Yeah. And I'm very… I think we are all sympathetic. My son has bipolar disease as well. He's been hospitalized twice on an acute basis. It's a very difficult thing as a family member to deal with. But in this case it's a very inexact science. The fault lies in the science. The fault lies in the variety or the specificity of the medications that are available—not in the decisions that we're making today to try and save money so that we can help people someplace else.

Jason Iltz: One of the things, Bill, before you start. This is Jason. As I listen to some of this testimony I've been biting my tongue when I hear the words "fail

first". And so I feel implored that I need to really speak on that because this has never been a policy where we have ever used the terminology of fail first. That is not what this is about. That particular… those words really are a tweaking or a twisting of what the intention is and that twisting has been done by the very advocacy groups that we've heard from today that are supposed to be representing their clients and their patients that they're serving. And so I feel that maybe there's… I need to speak to what I really feel is kind of an injustice here in that in order to serve these folks well, you know, we have to be giving them the most correct information.

If I say to my 11-year-old son, "Here's two medications on the table. The one on your left will work. The one on the right will not," which one will work for him? Pretty clear. I mean I've just told him which one will work for him. I haven't given him a fair opportunity to try one and if it doesn't work then to try the other one. He already has the pre-conceived notion that that medication won't work for him. And so what I would go back to and I would implore these folks to go back to the folks… it's very clear to your point ma'am that we have way more need than we have funds to meet all the need that's out there. We've gotta figure out a balance. And so, you know, if you can go back and give the information that's been presented here; it's not a fail first policy. It's a, "Hey, we have all these medications. They all have very severe side effects. It's not just one." Yes, EPS is an issue with some; maybe more than others. But I don't know that we know the whole story with all the newer agents. With Geodon it's right there. It prolongs the QT interval. So we can have cardiac issues. We've talked about weight gain. They are all so different.

If you can go back to the clients that you serve and that you represent and give them the facts and say, "Look, all of these medications that are out there there's really no way to know if they're going to work for you, but let's try one and let's see if it works. If it doesn't work we have others available to you." And if the policy is if we don't know let's try the one… I guarantee today if risperidone came out on the market today people would be lined up to get the newest and the best, latest and greatest. I don't understand why there's such a stigma with a medication that just because now it's generic all of a sudden it's not as good. Okay?

I'll get off my soapbox now but I really feel as though some of the advocacy groups need to go back to the clients that they serve, give them the facts. Okay? Don't tell them it's a fail first policy because it's not. We're not putting them on a medication to give them side effects. That's not the intent. We want to treat them to the best that we can and given the constraints that we have to work with, this policy seems to make sense. We will be able to treat more people in a very growing segment of population where there's a huge need.

Woman: I think in the real world part of the problem is that if somebody experiences symptoms, and normally it's not one symptom, it's many symptoms. But when people have symptoms from whatever medication at least in the community mental health system that I'm a part of, we go to or they come to us and want another appointment and that's going to be in three months. Okay? That's only going to get worse. Maybe they are lucky and they belong to an agency that's able to get them in in two months. But this person then has to sit with that set of symptoms that at times are very intolerable for a long time. It would be very different than any of us or most of us in this room where if I have a symptom I can call my doctor, I can email my doctor, I get a response within 24 hours. These people do not have that opportunity.

Barak Gaster: But there's no way for the prescribing doctor to know that some other drug that they wouldn't try first wouldn't have equally bad side effects and that you'd be in that same situation of not being able to get an appointment to get a different doc…

Woman: [inaudible]

Vyn Reese: This is Dr. Reese. I think we are sort of degenerating into an argument here. We've talked about these issues before. Bill, do you have anything to add to this?

Bill Struyk: Actually, just a point of clarification. Bill Struyk with Johnson & Johnson. What would be the effective date of the new EPA criteria?

Chuck Agte: If you're talking about the new EPA criteria for Invega Sustenna?

Bill Struyk: Yes, sir.

Chuck Agte: I think that that would depend on how quickly we're implementing all the changes within this class. I think we're trying for January 1st would be the earliest date that we could achieve both technically and for our publication requirements.

Bill Struyk: So January 1?

Donna Sullivan: That is the targeted date at this point in time. Yes, Bill.

Jeff Thompson: I apologize. I have to leave. I have to catch a flight to Spokane. But I just want to say thank you very much. I hope everybody can support this. It was done with legislative input and quite frankly I think you bring up an excellent point. If the message from Pharma and the advocates that this is a fail first model is what you're going to do, you've already doomed this program to failing first. This is not what I've ever said. This is not whatever my intention was. And if that's the message that the community wants then I think we are doing a disservice for my clients. So this is a generics first. I will promote it and if there is a problem, as I have done, I will be there and stand up to any community and take my licks if it's wrong. But I would hope, and this is a message to the drug companies and to the advocates, I would hope that you do not use the words "fail first". If you read the material that I presented to you, you can doom this program by using language and you do a disserve, I think, to our clients and DSHS.

Woman: [inaudible]

Vyn Reese: This is Dr. Reese. I think we've talked about this for quite a long time. We tried to allay your concerns in this very, you know, difficult times and in this difficult class of drugs. But I think if you had an open mind and you would just look at this open mindedly and look at what… all the safeguards that are in this program you would realize it's a well thought out program with a lot of data behind it and if somebody has a side effect that they need to be taken off the drug we can't… we can't fix all the problems with the mental health delivery system. Okay? It would be with any drug. If somebody is having side effects they have to sit on it for

three months. It's a tragedy, it's an outrage, but it could be with any drug—a brand name drug, a generic drug, any drug. And so that type of thing we can't address. But it's certainly… we don't know which drug is going to cause that side effect before they get it. Thank you.

Jeff Thompson: So again there's no action unless you want us to stop.

Vyn Reese: No action.

Jeff Thompson: This is an FYI for you. So thank you very much.

Vyn Reese: Great. Thank you very much for all your hard work. We appreciate it. Have a safe flight. Okay we're going to break… we're going to have a break for… again, we're behind schedule as usual.

Donna Sullivan: Dr. Reese, before you make your final announcement I do believe that Chuck does have something to address with clopidogrel. Even though Nichole's not here for her formal presentation, we would like some guidance on how to continue with that pro- or with our prior authorization. Chuck, you talk because I don't know what I'm talking about.

Chuck Agte: Yes. We do still intend to bring as the board requested information on the interaction of PPIs and clopidogrel. Nichole was not able to make it today so we are hoping to do that presentation at the next meeting. However, in the meantime we did want to address the fact that it was an edit that was originally put in place based on the preliminary information from the FDA and the board had not had input on it at that time. At this point in time, especially because of the delay in the presentation, and we would like to have your input with, you know, full information behind it. In the meantime we are requesting your support in going ahead and taking off the PPI and clopidogrel edit until you have had a chance to give us feedback after a full presentation.

Vyn Reese: This is Dr. Reese. I would commend that because I've had patients now with GI bleeds, three GI bleeds because their PPI was stopped and they couldn't get another PPI. So I think that we can't put that edit in place

and stopping all PPIs. Is that what it is now? That basically all PPIs are stopped?

Chuck Agte: Currently any PPI that comes through requires prior authorization if the client is already on clopidogrel.

Vyn Reese: And it's been very difficult to bypass that. To even prescribe pantoprazole it's been very difficult to bypass it and it's… I think it is putting patients at serious GI risk; especially patients who you know are already high risk to begin with from GI bleeds. So it's, you know, I think we're… I think it's a good idea to put that on hold until we have a chance to hear this. That's my personal view. I don't know what the rest of the committee thinks.

Donna Sullivan: Dr. Reese, I have a question. When you're saying the patients are having GI bleeds, are you specifically referring to patients on Plavix that are having GI bleeds because they could not get a proton pump inhibitor?

Vyn Reese: Because they have good indications for a proton pump inhibitor and they're on Plavix and therefore they have to stop taking proton pump inhibitors and they have had a history of previous… a lot of them are on combination aspirin and Plavix and they've bled on NSAIDs before and they bleed again.

Donna Sullivan: I just wanted to make… yeah, I understand.

Vyn Reese: So you take them off their PPI when they're on Plavix and if it's no PPI you can prescribe or it's very hard to get one. Then you put them at risk for GI bleeds.

Donna Sullivan: I was just wanting to get clarification that it was… that you were referring specifically to patients on Plavix because there is another proton pump inhibitor edit where after a patient's been on it for 90 days it does require a prior authorization to continue.

Vyn Reese: That is another…

Donna Sullivan: So I wanted to make sure that your comments were focused on the Plavix PPI interaction and that edit versus the ability to, you know, continue on a proton pump inhibitor after 90 days.

Vyn Reese: That's another edit I have a real problem with too because… we aren't discussing that right now.

Donna Sullivan: No, we were not. So I just wanted to clarify that…

Vyn Reese: Yeah. I can't get refills and PPIs after 90 days on my patients who have veritas esophagus with recurrent GI bleeds on… with erosive esophagitis and upper endoscopy. After 90 days I have to fight to get a PPI. So it's a very bad situation currently and it needs to be rectified. But that's not what we're talking about.

Donna Sullivan: I was making sure that you weren't broadening your comments about GI bleeds.

Vyn Reese: No. But I could if you ask me. But it's not…

Donna Sullivan: We'll save that for another day. Thank you.

Vyn Reese: All right. So any other discussion? So the committee's in agreement with your plan is not to do that. Now we're adjourned for five minutes. Five minutes. Okay.

Okay. This is Dr. Reese again. I'd like people to take their seats. We're going to reconvene as the Washington State Pharmacy and Therapeutics Committee and resume our drug class review scans.

So the first drug class review is on the triptans and I will be reading it given the OHSU meeting today. This is drug class review on triptans. It's update 5, preliminary scan 1. Next slide, please.

History date of last update was update number 4, completed June 2009. Next slide.

Inclusion criteria – populations: adult patients with migraines. Interventions: were all forms of almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, sumatriptan-naproxen fixed-dose combination product and zolmitriptan. Next slide.

Inclusion criteria continued – effectiveness/efficacy outcomes: pain, nausea, vomiting, photophobia, phonophobia, functional outcome, quality of life and consistency. Harms were overall adverse events, withdrawals due to adverse events, incidence and withdrawals due to specific adverse events. Slide number 5.

FDA and Health Canada website searches – new drugs are none. New indications – almotriptan is now indicated for migraines in adolescents as of May 2009. Safety alerts – there are no new black box warnings. Slide number 6.

Medline search – date range: January of 2009 through April of 2010. Total new citations founds in this scan are 30. Number 7.

Study selection – new potentially relevant trials are 5. Head-to-head trials are one; almotriptan versus rizatriptan. Placebo-controlled, active control trials are 4; eletriptan on work productivity, quality of life; frovatriptan on consistency over multiple attacks; rizatriptan ODT and early treatment; sumatriptan/naproxen fixed-dose combination use… that's for use in poor responders to triptans. Slide number 8.

And that's it. I'll take a motion from the committee to accept the scan.

Susan Rowe: Susan Rowe. I move to accept the scan.

Vyn Reese: Is there a second?

Carol Cordy: Carol Cordy, I second.

Vyn Reese: All those in favor say, "Aye."

Group: Aye.

Vyn Reese: Opposed, same sign. There is one stakeholder that would like to speak and that's Dr. Jennifer Brzana from GlaxoSmithKline, PharmD.

Man: [inaudible]

Vyn Reese: Thank you. I will now turn your attention to the motion from the last time. Looks like the drugs are pretty much the same. There are new formulations of the drugs, but they are the same drugs.

Susan Rowe: Susan Rowe. In looking at this motion though it does not address use in adolescents and we do have one new study.

Jason Iltz: We haven't reviewed that evidence. So I don't know that we need to change our motion based on that. I mean when we're… I think we're reiterating our prior motion after having said that there's maybe a little bit of data out there that we haven't yet reviewed.

Carol Cordy: This is Carol Cordy. Can… maybe Jeff you can clarify for me. How are the… I'm sure we've talked about this before, but how are the decisions made as to whether to have a complete new review or just a scan?

Jeff Graham: Well, the DERP participating organizations make that decision. I don't think we're going to have a complete update of this drug class. I'm pretty sure we're not. And so if you decide that you want us to do one I mean the State of Washington could do that by themselves, but probably not right now because we literally wouldn't have the money to do that.

Carol Cordy: I was just curious as to who... where that decision comes from.

Jeff Graham: You know, and the other thing I wanted to point out the sumatriptan/ naproxen was actually provided to us… oh yeah, we do have it there, last October.

Patti Varley: This is Patti Varley. We have in the past if there are only certain drugs approved for the use in specific populations, i.e. children or adolescents we have made a comment within the context of the motion that said that one had to be on the Washington Preferred Drug List because it was the one approved for that age group. So we could…

Donna Sullivan: So this is Donna Sullivan. So I want to add to what you said Patti. You have said in the past, if you directed us, like in the previous class with the antihistamines to have a product that is, you know, approved for children then we can treat that as a subclass and then we can make that available only to children. So it's not used in adults before another product might be used that is also indicated in adults.

Jeff Graham: Do we know that none of the other drugs are… have been approved for adolescents?

Donna Sullivan: Off the top of my head I don't know which drugs are approved for which age groups at this point in time.

Susan Rowe: Susan Rowe. I also am not aware of any triptan trials under 18.

Vyn Reese: This is Dr. Reese. I don't think we know. We would need a full review I think to know. It would be unusual for one triptan to work in adolescents and another triptan not to work since they all work differently in different percentages of people. It's hard to know whether they have been studied in other… there are other studies in adolescents. I don't know that off the top of my head.

Donna Sullivan: This is Donna Sullivan. Just because it's been studied in children they may not have an FDA indication for the use in children in that age.

Patti Varley: But according to this slide, if I read it correctly, that's why I'm commenting is that this one, like we've dealt with in other class, because we don't have data about class effect where there have been individual agents that have been studied and FDA approved in children and adolescents. This one does. That's what the slide says. It's FDA indicated for adolescents and I don't think we have that with any of the others.

Chuck Agte: This is Chuck Agte and that would be similar to other motions you've made in the past. That would be a reason why within your motion you might say rather than picking a specific drug you must have something with pediatric indications as preferred.

Jeff Graham: Do we stop these drugs for adolescents?

Chuck Agte: Not currently. Usually what happens is in the event that drug in question might otherwise be non-preferred we create expedited authorization criteria so that the PDL rules do not apply for certain age ranges. So it's less a matter of stuffing them for children and may… as opposed to making sure the window is open for a prescriber to use the one that is indicated within that age range.

Patti Varley: The other comment I would make is if we stated in that language that it must include those approved for FDA use in children and adolescents. It does leave open the opportunity that if other ones do do the studies necessary to get FDA approval they could be added without us having to change the motion.

Woman: Or that a study does exist that we don't know about.

Donna Sullivan: So at this point in time with the changes…

Woman: With FDA approval.

Donna Sullivan: So at this point in time with the decision that there won't be changes made to the PDL for several months unless you tell us or change the motion to say we must have a product preferred that is FDA approved for pediatric use then there would not be a change. There's nothing that would prevent a drug from being used in pediatric patients at this point in time. But I believe that this product is not preferred currently.

Chuck Agte: Yes, that would be the differences that it's not that the product is specifically being stopped for children, but if it's non-preferred it's non-preferred. And so if you wanted to open that window it's something that we would have to do as a separate action.

Donna Sullivan: That is correct. And so in the past…

Vyn Reese: We haven't had a full review of this indication.

Donna Sullivan: No, you have not. Okay.

Barak Gaster: This is Barak Gaster. I feel like we don't know enough about whether any of the triptans are really different from any of the other triptans for use in adolescents to put a statement like that in our motion. I think that we are all… we are all appropriately skeptical about whether something has a pediatric indication or not; whether that really means that it is any safer in the use of pediatric populations in any of the drugs that don't have such an indication in a class where all the drugs are generally so similar in terms of their side effect profile, that I would… I would advocate for not having that in the motion.

Vyn Reese: Okay. So given all that discussion who wants to either make this a motion as a re-do of the prior one or modify it in some way?

Carol Cordy: This is Carol Cordy again. Because there's one new drug, the combo, the sumatriptan/naproxen…

Patti Varley: No. That was reviewed last time.

Vyn Reese: We already dealt with that last time on the bottom.

Carol Cordy: Oh. So it's not going to be included in the class.

Chuck Agte: That's part of the reason that in your previous motion you specifically referred to triptan monotherapies.

Carol Cordy: Okay. Thank you.

Barak Gaster: This is Barak Gaster. I think the only change we would make would be that we haven't… the first line we haven't considered updated evidence as we did in October of 2009. Since this is just a scan so rather than reiterating the prior motion I would say we would reiterate it except for just that… we would take that first line out. And so just saying, "After considering the evidence of safety and efficacy and special populations for the treatment of migraine, and then reiterate the rest of it exactly as it was. But just take out "updated evidence" or just take out "updated" because we didn't update the evidence this time. So I would make that motion.

Vyn Reese: Any other discussion?

Patti Varley: This is Patti Varley. I'm struggling with the child part just because I think a lot of pediatric people… we function off label all the time and I agree from a scientific point of view that we have no evidence one way or the other but when one does get FDA approved for kids, for me, that is an issue. So I just want to state that for the record.

Deb Wiser: This is Deb Wiser. I agree with Patti on that. If I have a choice among triptans I would prefer to use the one that's on label for that age group then do something that was off label.

Donna Sullivan: And this is Donna Sullivan. I just want to remind… they are subject to therapeutic interchange. So if you do have a child and you write for that product and write "dispensed as written" it would be… if you're an endorsing provider it would be covered with no prior authorization. So it's available. It's not… but it's just not listed as a preferred agent. But prescribers do have access to it.

Deb Wiser: Okay. Then this is Deb Wiser. I second.

Vyn Reese: All those in favor say, "Aye."

Group: Aye.

Vyn Reese: Opposed, same sign.

Patti Varley: Aye.

Vyn Reese: So one opposed. The next item on the agenda is the scan review on drugs for Alzheimer's disease. This is Dr. Reese. Drug class review on drugs for Alzheimer's disease update number 2, preliminary scan number 4, September 2010.

History – originally report was in April 2005. Update number 1, June 2006 with searches through December 2005. Previous update scans are

update number 2, scan number 1, June 2007; update 2, scan number 2, May 2008; update 2, scan number 3, June 2009. Number 3.

Inclusion criteria – population: patients with Alzheimer's disease. Number 4.

Inclusion criteria – interventions: donepezil (Aricept), galantamine (Razadyne, formerly Reminyl), memantine (Namenda), rivastigmine (Exelon), tacrine (Cognex). Number 5.

Inclusion criteria – effectiveness outcomes: stabilizing or slowing the rate of decline in health outcomes measures (e.g., ADLs or QOL). Intermediate outcome measures (cognition, global assessment). Number 3, caregiver burden. Number 4, hospitalization or nursing home placement and lastly mortality. Harms are adverse events, withdrawals and specific adverse events. Number 6.

FDA and Health Canada website searches – new drug approvals: 6/21/2010 Namenda XR (memantine hydrochloride) 7 mg, 14, 21 mg and 28 mg extended release capsules. Number 2, 7/6/2007 Exelon Patch (rivastigmine transdermal system). No new safety alerts. Number 7.

Medline search date range June 2009 to August 31, 2010. Total new citations found in this scan were 75.

Potentially relevant new trials – donepezil versus memantine (trial in progress). Switching from donepezil tablet to rivastigmine transdermal patch and pooled analysis from 3 placebo-controlled trials of donepezil. Previous scans identify 85 additional potentially relevant trials. Number 9.

And that's it for this scan. I'll take a motion to accept the scan.

Christine Klingel: This is Christine Klingel. I move to accept the scan.

Carol Cordy: This is Carol Cordy. I second.

Vyn Reese: Okay. The motion has been made and seconded to accept the scan. All those in favor say, "Aye."

Group: Aye.

Vyn Reese: Opposed, same sign. Scan is accepted. Let's turn our attention now to the prior motion. Is there stakeholder input, too? Let's make sure we do that. Reene Prather, PharmD and I can't read where you're from.

Reene Prather: I'm Reene Prather, PharmD from Aisai Medical Affairs and thank you for the opportunity. I want to provide an update on new formulation for Aricept. Aricept is a reversible inhibitor of the enzyme acetylcholinesterase and it's the only Alzheimer's drug that is approved for all stages of Alzheimer's disease. It's available as a once-a-day regimen in 5, 10, and 23 mg tablets, 5 and 10 mg oral disintegrating tablet. These doses are indicated 5 mg a day for mild to moderate, 10 mg for mild, moderate and severe, and the 23 mg a day for moderate to severe Alzheimer's disease. This was approved by the FDA the end of July this summer. All patients are started on a dose of 5 mg a day, which may be increased to 10 mg after four to six weeks. Patients must receive the 10 mg dose for three months before advancing to the increased dose to 23 mg per day. We have pivotal trials in the 5 and 10 mg and I wanted to speak to the results of a controlled clinical trial in over 1,400 patients with… pardon me, comparing Aricept 23 mg to 10 mg once a day. This is in the moderate to severe category. It is suggested that the 23 mg dose provided additional benefit on cognitive performance which was assessed by the severe impairment battery. It did not show a statistically significant difference in global function measured by the cibic(?) but it was trending.

In addition to the pivotal trials short-term and long-term efficacy trials with Aricept 5 and 10 have demonstrated that Aricept maintains the activities of daily living, helps to keep the patients in the community, and helps to promote behavioral symptoms and associated caregiver distress.

I also want to bring light to some of the important safety information for this drug. Like all the cholinesterase inhibitors it does have the potential to increase gastric acid secretion. Sinkable episodes have been reported

associated with the use of Aricept. It should be used cautiously in patients undergoing anesthesia and with certain pre-existing conditions such as bradycardia, seizure disorder, asthma COPD and bladder outflow disorders.

Aricept 23 has been associated with weight loss. So consideration should be given when prescribing this 23 mg dose to patients with lower body weight. In the clinical trials the most adverse common events were nausea, diarrhea, insomnia, vomiting, muscle cramps, fatigue and anorexia. With the 23 mg a day they have had more incidents of the nausea and vomiting than what you saw when it was compared with…

Jeff Graham: Please conclude your remarks.

Reene Prather: I'm done. Thank you so much for this opportunity.

Vyn Reese: Thank you. Any questions from the committee or comments? We haven't reviewed this data on the Aricept 23. It wasn't in this update.

Reene Prather: Correct.

Vyn Reese: And the GI toxicity is dose related and in that severely demented group, this is a comment, they are already losing weight and you usually don't usually want to give them something that's making them lose more weight. And I'm very concerned about that possible side effect as an aside.

Reene Prather: I understand. Yes.

Vyn Reese: That's of great concern. But I appreciate your presentation.

Reene Prather: And I think it's important to go back to the comment… or the note in the PI that says if you move from 5 to 10 mg; when you are at 10 mg you should be on that as a stable dose for three months. So I think it would speak to looking at those patients that would be at risk for increased weight loss.

Vyn Reese: Okay. Thank you.

Reene Prather: Thank you.

Vyn Reese: Next patient… or next… next presenter is Dr. Elson Kim from Forest Research Institute.

Elson Kim: Good afternoon. My name is Elson Kim representing Forest Labs and Namenda for the treatment of Alzheimer's disease. As you already know Namenda is safe and efficacious in the treatment of Alzheimer's patients with moderate to severe disease both alone and in combination with a cholinesterase inhibitor. It is the only FDA approved glutamate pathway modifier in the USP motto guidelines under the therapeutic category of anti-dementia agents.

Two of the trials that I want to speak to you today is (1) if you ask a rhetorical question, "Is there any [inaudible] data to support guidelines for the duration of therapy with anti-dementia drugs?" This question was answered by Susan Roundhouse et al in a study called Persistent Treatment with Cholinesterase Inhibitors and/or Memantine Slows Clinical Progression of Alzheimer's Disease. The conclusion reads, "Persistent drug treatment had a positive impact on Alzheimer's disease progression assessed by multiple cognitive, functional and global outcome measures. The magnitude of the treatment effect was clinically significant. Positive treatment effects were seen even found in advanced disease."

The second study I wanted to bring your attention to, this was also in 2009 by Autry(?), titled Long-Term Course and Effectiveness of Combination Therapy in Alzheimer's Disease. They comment, "Long-term real world clinical effectiveness data for monotherapy or combo therapy is lacking." Quote again, "There are no published studies that have passed, assessed and compared the effects of cholinesterase inhibitor monotherapy and cholinesterase inhibitor plus memantine combination therapy in real world setting for durations greater than one year." We fast forward to the discussion section of the paper and I'm quoting, "Combo RX is superior to no RX and cholinesterase therapy monotherapy. Further the clinical benefits of combo therapy are sustained for at least two years." And quote again, "For untreated

patients the expected mean rate of deterioration on the blessed dementia scale is in the range of three to four errors per year. Our results predict that on average cholinesterase inhibitor monotherapy decreases this deterioration by about one error per year and that combination Rx therapy decreases it by two errors per year."

The most common adverse events with memantine are dizziness, confusion, headache and constipation and in patients with severe renal impairment a dosage reduction is recommended. Caution is advised in patients with severe hepatic impairment or under conditions that raise your pH.

To close, patients treated with memantine for moderate to severe Alzheimer's disease has shown improvement on cognitive, functional, communication, behavioral and global measures. Memantine is safe and well tolerated and can be used effectively as monotherapy or in combination with cholinesterase inhibitors. Thank you.

Vyn Reese: Thank you. Any questions from the committee? Okay. Thanks. So now we'll turn our attention to the motion before us. Does anybody want to just reiterate that motion?

Jason Iltz: This is Jason. I'd like to reiterate the motion from October 21st, 2009 as it's listed.

Vyn Reese: Is there a second?

Barak Gaster: This is Dr. Gaster. I second it.

Vyn Reese: Any discussion? All those in favor say, "Aye."

Group: Aye.

Vyn Reese: Opposed, same sign. It's passed.

The next drug class review is on newer antiplatelet agents. It is also a scan. Drug class review in new antiplatelet agents, update 2, preliminary scan 3, April 2010. Slide 2.

History – date of last update: update number 1 was in April 2007. Dates of previous preliminary updates were preliminary update scan number 1 was in March 2008 and preliminary update scan 2 was in June 2009. Slide 3.

Inclusion criteria – populations: adults with acute coronary syndromes, recent or ongoing coronary revascularization by stenting or bypass grafting, prior ischemic stroke or transient ischemic attack, symptomatic peripheral vascular disease. Interventions: clopidogrel (Plavix) alone or in combination with aspirin, Ticlopidine (Ticlid) alone or in combination with aspirin, Dipyridamole (Persantine, generic brands) in combination with aspirin and Dipyridamole ER in combination with aspirin (Aggrenox). Number 4.

Effectiveness outcomes: all-cause mortality, cardiovascular mortality, myocardial infarction, stroke and failure of an invasive vascular procedure. Safety outcomes: overall adverse effect reports, withdrawals due to adverse effects, serious adverse events reported and specific adverse events. Number 5.

Medline search – date range: May 2009 to April 2010, presugrel extended back to 1948. New total citations found in this scan were 162. Number 6.

FDA and Health Canada searches – new drugs: Prasugrel (Effient) approved on July 20, 2009. New indications are none.

FDA and Health Canada searches – safety alerts on clopidogrel, which we already discussed. Black box warning added in March 2010. Warning of diminished effectiveness in patients who are CYP2C19 poor metabolizers. Number 8.

Current scan: new potentially relevant trials. The Dengler EARLY trial population was ischemic stroke, comparison was aspirin plus ER Dipyridamole versus aspirin. Study 2 was Uchiyama 2009 Japanese stroke patients' clopidogrel versus Ticlopidine. Number 3 was Wiviott 2005 JUMBO-TIMI-26 population was PCI patients Prasugrel versus

clopidogrel and Wiviott, 2007 TRITON-TIMI 38 ACS with scheduled PCI Prasugrel versus clopidogrel.

Study selection continued. Current scan: study analyses of trials 4 secondary analysis of TRITON-TIMI 38 trial, 4 secondary analysis of CHARISMA trial. Prior scans: new trials 7 and secondary analyses 11. Number 10.

And that brings us to the end of that scan review. I'll take a motion to accept the scan.

Deb Wiser: Deb Wiser. So moved.

Vyn Reese: And a second.

Barak Gaster: Barak Gaster, I second.

Vyn Reese: All those in favor say, "Aye."

Group: Aye.

Jeff Graham: Vyn, this is Jeff Graham. I just wanted to let the committee know that a full update is being done on this drug class. It will be done… completed in about I think June or July of 2011.

Vyn Reese: So that's going to be in a while?

Jeff Graham: Right. They will do it again in a year.

Vyn Reese: Right. So we'll look at this motion but we'll also get some input from stakeholders. The first stakeholder is Rhalene Patavo from Boehringer Ingelheim.

Rhalene Patavo: Hi. My name is Rhalene Patato. I'm a Pharmacist and a Medical Liaison with Boehringer Ingelheim. I'm on the respiratory side because my cardiovascular colleagues could not be here today, but I wanted to provide some of the changes that are relevant from the package circular. As you know Aggrenox is indicated to reduce the risk of stroke in patients

who have had a transient ischemia of the brain or completed ischemic stroke due to thrombosis. It is one capsule b.i.d. It is not interchangeable with the individual components of aspirin and dipyridamole tablets. In the ESPS 2 trial Aggrenox showed a statistically significant 22% relative risk reduction for stroke versus aspirin. In that same trial Aggrenox had similar bleeding rates to low dose aspirin.

There's an increased risk of headache with dipyridamole compared to placebo. Studies with extended release dipyridamole show that headache is generally mild and transient. In the event of an intolerable headache during initial treatment, patients may be switched to one capsule of Aggrenox at bedtime and one low dose aspirin in the morning. And patients should return to their usual dosing regimen as soon as possible since no outcomes data is available, usually within one week.

Aggrenox does contain aspirin. So patients who consume three or more alcoholic beverages a day should be counseled about the increased bleeding risks with chronic heavy alcohol use while taking aspirin and also those with a history of PUD should also avoid aspirin.

Aspirin is contraindicated in patients with known allergies to NSAIDs and patients with the syndrome of asthma, rhinitis and nasal polyps in combination. Aggrenox should also be avoided in the third trimester of pregnancy.

The 2008 AHA guidelines update recommends the combination of aspirin and extended release dipyridamole as an acceptable initial therapy for reducing the risk of stroke in patients with non-cardio embolic ischemic stroke or TIA. And if you have any questions I'd be happy to forward them on to our team.

Vyn Reese: Thank you. Any questions from the committee? Thanks. Next up is Steve Cheng from Eli Lilly. On deck Dan James from Bristol-Myers Squibb.

Steve Cheng: Good afternoon, again. My name is Steven Cheng. I'm a Health Outcome Liaison with Eli Lilly. I would like to speak on behalf of Effient or prasugrel. Effient is a new thienopyridine indicated to reduce the rate of thrombotic cardiovascular events including stent thrombosis in

patients with ACS or to be managed with PCI as follows: patients with unstable angina or non ST elevated MI, patients with ST elevated MI when managed with primary delayed PCI.

The clinical evidence for the effectiveness of Effient is derived from the TRITON-TIMI 38 trial. A 13,608 patient multi-center international randomized double blind parallel group study comparing Effient to a regiment of clopidogrel; each added to aspirin and other standard therapy in patients with ACS who were to be managed with PCI. Effient in comparison to clopidogrel proved to have a statistically significant difference when considering the primary composite endpoint of CV death, non-fatal MI or non-fatal stroke in the following patient populations. Effient was primarily driven by a reduction in non-fatal MIs and the effect of Efficient within various pre-specified subgroups was generally consistent and favored Efficient with the exception of patients with a history of TIA or stroke.

There were 50% fewer stent thrombosis among patients randomized to Efficient. Pharmacokinetics are the act- tablet… Effient are not known to be affected by genetic variations in cytochrome 2C19, 2B6, 2C9 or cytochrome 385. Effient can be administered with aspirin, heparin, glycoprotein 2B3A inhibitors, statins, [inaudible] and drugs that elevate gastric pH including proton pump inhibitors.

The primary safety endpoint of non-[inaudible] TIMI major bleeding was significantly higher in the Effient arm than in the clopidogrel arm. Non-[inaudible] TIMI major and minor bleeding was significantly higher in the Effient arm than in the clopidogrel arm. Adverse reactions-related drug to discontinuation with 7.2 for Efficient versus 6.3 with clopidogrel.

Contraindications – Efficient is contraindicated in patients with history of prior TIA or stroke. Efficient is contraindicated in patients with active pathological bleeding such as peptic ulcer or intracranial hemorrhage. I would like to respectfully ask that Effient be considered for the Washington PDL.

Vyn Reese: Okay. Thank you. Are there questions from the committee? One comment. This is not a total review. This is just an update scan and we'll

have a total review later. The concern about serious GI bleeds with Effient is, I guess, still to be resolved. There's phase 3 trials in progress and there's no morbidity or mortality benefits as I understand it right… currently. So I think we'll probably delay that until we have a complete review after the trials are in.

Man: [inaudible]

Vyn Reese: That's true. So I mean if somebody prescribes it in an in-patient basis then they could… if they're an endorsing provider I don't know if they are going to be able to get it. That's the question. But I think there's a lot of questions about the drug currently.

Donna Sullivan: This is Donna Sullivan. Since it hasn't been fully reviewed and included in the drug class it is not considered a part of this class for purposes of therapeutic interchange. However, each of the agencies can, you know, cover it or not cover it. Not necessarily not cover it; cover it according to their benefit design or business model.

Vyn Reese: Any other discussion? Okay. One more person, sorry. Dan James?

Dan James: Yeah. I'm Dan James. I'm from the Medical Department of Bristol-Myers Squibb and also representing Sanofi-Aventis. I'll be very, very brief. We've had two changes to our package insert. One is the box warning, which you showed in your documents so I won't say anymore about that. The second is a positive change with more data concerning the PPI clopidogrel interaction, which is actually word-for-word in the document that was prepared in the pharmacy that I saw there. So I just want to bring that to your attention and with that I'd be happy to answer any questions that you have regarding any of that data. Thank you very much.

Vyn Reese: Okay. Thank you. Any questions? Okay. Let's look again at the antiplatelet motion.

Susan Rowe: Susan Rowe. I move to reiterate the present motion.

Deb Wiser: Deb Wiser. I second.

Vyn Reese: The motion has been made and seconded to reiterate the prior October 21st, 2009 statement. Any discussion? All those in favor say, “Aye.”

Group: Aye.

Vyn Reese: Opposed, same sign. Is there any other business before the committee? Then we’re adjourned.